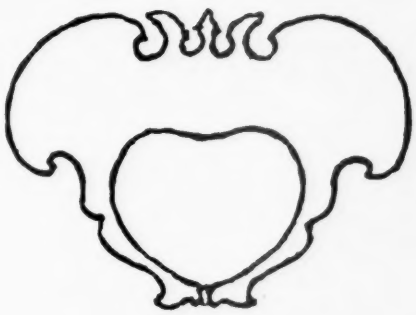
American Journal of Obstetrics and Gynecology



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Twenty-Fifth Anniversary

THE AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY 1920-1945

TWENTY-FIVE years ago, in October of 1920, the first issue of the JOURNAL appeared as the successor of a periodical founded in 1868, the "American Journal of Obstetrics and Diseases of Women and Children," which ceased publication in 1919 after a notable career.

The work of these two journals together has covered an uninterrupted period of seventy-seven years, during which the specialty of obstetrics and gynecology has been represented by a monthly periodical devoted exclusively to its interests. Seventy-seven years is a long time. In this period the specialty has become transformed. The diseases of children as covered in the former "Blue Journal" no longer come within the domain of the doctor who confined their mothers. Moreover, the distinction between the gynecologist and the obstetrician is gradually disappearing and a great single branch of medicine has developed, formed from this fusion. The mechanical and surgical procedures, so important in the earlier history of obstetrics and gynecology, have become somewhat standardized, and the new interests of the specialty stem especially from the physiologic problems of the reproductive process.

During this past quarter of a century, medicine has participated in the revolutionary changes which have affected the entire world. We have seen, above all, the effort to make medical advances more available to all of the people, with a resulting expansion of governmental direction and control. The extension of direct medical service to a certain group of the people, as exemplified by the Emergency Maternity and Infant Care program, may be but the first of a succession of projects by which maternity care finally is to be provided through governmental funds for any woman who requests it. It is understandable that the fields of obstetric and pediatric practice should be the first to receive such attention, for there is a sentimental factor involved in caring for the Nation's mothers and children. These special fields may, however, serve simply as an area in which such measures are the first to be tried, and serve as a forerunner,

perhaps, of the extension of government activity in other branches of medicine. Whether such expansion from previous accepted methods will prove either desirable or beneficial is for the future to decide. There remains a lingering doubt in the minds of many physicians whether such measures, centrally controlled in the final analysis by a bureaucratic administration in the national capitol and supported by universal taxation, will bring about that practical ideal in maternal and infant welfare which we all desire.

In these last two and one-half decades of great social, political, economic, and scientific developments, medicine has occupied a leading role. Within the domain of the specialty embraced by the JOURNAL, signal advances may be recorded. Knowledge of the physiology of reproduction has advanced greatly, with the attainment in particular of a knowledge of the role of the endocrines, the morphologic development of the embryo, and the control of uterine contractility. Gynecologic and obstetric pathology has become an essential part of the personal knowledge of each practitioner of the specialty. The widespread use of blood and plasma has completely altered the outlook in major surgical operations and in obstetric hemorrhage. The sulfonamides and penicillin have revolutionized the treatment of infections. Radiation has been further developed in the treatment of cancer. Finally, the enlistment of the efforts of the practitioner of obstetrics in a great cooperative study has produced a phenomenal improvement in obstetric mortality and morbidity.

Of interest is the fact that the mechanical phases of gynecologic treatment show little change while the development of medical and physical methods of therapy and diagnosis has assumed such great prominence. While operative technics have been developed and expanded, the scalpel today is less in evidence than the test tube, the experimental and the research laboratory.

The JOURNAL has endeavored to keep pace with these developments. Its pages have reflected the progress of the specialty throughout our country and we feel that it has functioned satisfactorily as an organ for the dissemination of the new developments in its field. We are proud of this record and proud likewise to acknowledge the faith which our contributors and subscribers have had in the JOURNAL. The catholicity of its contents and the number of its readers are attested by the quoted references from its articles which have permeated American and foreign medical literature.

At the close of a quarter century of personal service to the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, I want to commend the efficiency, liberality, and courtesy of our publishers, The C. V. Mosby Company. I am also proud to give recognition to the helpfulness and faithfulness of my associates, the late and lamented Dr. Hugo Ehrenfest, and Drs. Howard C. Taylor, Jr., and William J. Dieckmann, my immediate co-workers. Appreciation is likewise due to Dr. Robert T. Frank, the Editor of the Book Review Department, and to the staff of abstracters who have so efficiently recorded the world's literature in this field. To the members of the Publication Committee and to the Advisory Editorial Board an acknowledgment is also extended for their ever-ready cooperation.

George W. Kosmak, M.D.

THE PATHOGENESIS OF POSTSALPINGECTOMY ENDOMETRIOSIS IN LAPAROTOMY SCARS

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THE pathogenesis of endometriosis in laparotomy scars is not the same in all cases and its positive solution in a given case may be difficult or even impossible. It depends greatly on the type of the original operation and the anatomic conditions or relations resulting from it.

The progress already made toward a better understanding of the pathogenesis of scar endometriosis as well as the need for further studies are shown in the following brief historical review of this subject.

The first recorded case of endometriosis in a laparotomy scar was published by Meyer[1] in 1903. In keeping with observations made in the cases reported in the present paper, his case also followed salpingectomy and ventrofixation of the uterus. He believed that the endometriosis in his case arose from adenomatous changes in the uterine serosa in contact with the scar.

Von Franque[2] was the first to suggest that scar endometriosis might arise from the growth of bits of uterine mucosa transplanted into the abdominal wound. His case, reported in 1916, followed the repair of a perforation of the uterus caused by ovum forceps employed in the termination of an early pregnancy.

In the year 1926, Nicholson[3] was able to collect only 28 cases from the literature. Fifteen of these followed ventrofixation of the uterus. He claimed that the continuity between the uterine mucosa and that of the growth in the laparotomy scar had not been established in a single instance in these cases and believed that the serosal theory offered the fewest difficulties in explaining the origin of the ectopic endometrial tissue.

In the year 1928, the writer[4] reported two cases of endometriosis of abdominal scars following tubal sterilization and the extraperitoneal fixation of the fundus of the uterus in the abdominal wound. In both patients the uterus and the abdominal scar were removed at the second operation without disturbing the relation between the two. The microscopic study of sections, which included both the endometriosis of the scar and the portion of the uterus fused with it, in each case demonstrated that sprouts from the mucosa of one of the tubal stumps had invaded the uterine cornu and from there penetrated the abdominal scar. As far as I can ascertain, these are the first cases in which a continuity between normally situated Müllerian (tubal) mucosa and that in laparotomy scars has been reported.

In the year 1929, Hosoi and Meeker[5] collected 87 cases. They presented a valuable abstract of these cases which were arranged chronologically. Thirty-seven of them followed ventrofixation of the uterus. They stated that "in those in which the fundus uteri was ad-

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herent to the tumor mass in the laparotomy scar, serial sections could demonstrate no endometrial tubules in the adherent portion of the uterus. This shows the laparotomy tumors in the literature were not due to an extension from the uterine cavity.'' They also stated, ''The transplantation theory seems to explain the majority of the cases, as most occurred after operation on the uterus and adnexa. The serosal metaplasia and the lymphatic theory have been applied to those instances in which a simple appendectomy has been performed and in which there was no hernia.''

In the year 1930, Haselhorst and Otto[6] reported 27 cases of endometriosis in laparotomy scars, 24 of which occurred after ventrofixation of the uterus. They believed that the endometriosis in all of these 24 cases was continuous with either the uterine or the tubal mucosa. In 14 cases they excised the tumor in the scar with the portion of the uterine wall adherent to it. By means of careful microscopic studies of this tissue they were able to demonstrate a continuity between the uterine or tubal mucosa and that in the endometriosis in the scar, frequently in the vicinity of silk threads employed in the fixation of the uterus. Their observations confirmed those which had been reported by me[4] in 1928.

In the year 1930, two additional cases of scar endometriosis were reported by the writer.[7] In the first one, the uterus, after both tubes and ovaries had been severed from their uterine attachments, had been drawn through the abdominal incision and its fundus fixed in the subcutaneous portion of the abdominal wall. At the last operation, twelve years later, the body of the uterus, together with a mass of indurated adipose tissue about each cornu, was removed and a ventrofixation of the cervix done. The uterine cavity was injected with gelatin containing graphite. In the microscopic study of the right cornu and the tissue about it, graphite was found in the lumina of Müllerian tubules in the tissue beyond the tubal stump. More sections demonstrated that tubules, which now contain graphite in their lumina, had actually sprouted from the traumatized tubal mucosa and had invaded the tissue about the stump. A similar study of the left uterine cornu was even more interesting. Normal healing of this tubal stump had occurred without any tubules from its mucosa growing out into the surrounding tissue, and graphite was not found in the lumina of the Müllerian tubules about it. It was inferred that the endometriosis about this stump, with a histologic structure similar to the preceding one, might have arisen from the growth of tubal mucosa transplanted in the wound at the time of the previous operation. The injection of the uterine cavity with graphite proved to be of the greatest value in ascertaining the pathogenesis of the endometriosis of the abdominal wall in this case.

In the second case the uterus had been fixed in the abdominal wound after removing both tubes and one ovary. At the last operation, four years later, the uterus and the laparotomy scar were removed. The uterine cavity was injected with gelatin containing bismuth subcarbonate. The specimen was studied in the same manner as the previous one. The scar endometriosis was fused with the center of the fundus and not with either uterine cornu, although stump endometriosis, in which the tubules contained gelatin, was present in both. Further evidence found in the study of this specimen indicated that the scar endometriosis had probably been derived from the uterine mucosa by continuous invasion in the attempted repair of a rent in the uterine wall probably caused by a ventrofixation suture which had penetrated the uterine cavity. Gelatin was not found in the scar endometriosis. When gelatin is present in cavities of scar endometriosis, we know they are continuous with the uterine cavity. When it is not found in any of these ectopic cavities, the origin of the scar endometriosis from the mucosa of a stump or fundus has not been positively excluded.

In the year 1934, Harbitz[8] published an excellent monograph on scar endometriosis. He had collected from the literature 193 cases of endometriosis in laparotomy scars, of which 81 followed ventrofixation of the uterus, often combined with other operations on the pelvic organs. Only one of his own 15 cases followed ventrofixation of the uterus. In the remaining 14, two followed cesarean section at term, and 12 hysterotomy for the termination of early pregnancy. He states that in Norway ventrofixation of the uterus is rarely employed, while hysterotomy for the termination of early pregnancy followed by tubal sterilization is a relatively common procedure.

In the year 1941, Wespi and Kletzhändler[9] published a paper on cicatricial endometriosis. They commented on its rarity, stating that only 390 cases had been reported in the literature. Seventy-three instances of this condition had been encountered during the preceding sixteen years at the Zurich Clinic. Five of these followed cesarean section at term and 68 followed abdominal hysterotomy for the termination of early pregnancy. They believe that the transplantation of bits of uterine mucosa into the abdominal wound is the only possible explanation of the endometriosis in their cases. In support of this view, they report that since they have been employing a technique which, during the operation, lessens the soiling of the abdominal wound with the contents of the uterus, the incidence of scar endometriosis has been greatly reduced. With Harbitz, they believe that the endometrium of early pregnancy is more viable than that of pregnancy at term. Their observations have greatly strengthened the theory that bits of uterine mucosa transplanted in the abdominal wound may sometimes live and cause endometriosis in the scar. This phenomenon might easily have occurred in many of the reported cases which have followed other pelvic operations.

In the year 1942, Wyrens and Randall[10] reported 31 cases of endometriosis in laparotomy scars occurring in the Mayo Clinic from the years 1916 to 1941. The preceding operations in these cases were: uterine suspension, 15; cesarean section, 4; salpingectomy, 4; hysterectomy, 2; myomectomy, 2; drainage of an appendical abscess, 1; appendectomy, 1; inguinal herniorrhaphy, 1; "pelvic operation," 1. "In 10 of the 31 cases the tumor in the abdominal wall was found to involve or was adherent to the uterus or tubes. Eight of these tumors involved the uterus alone; one was continuous with an endometriosis which involved the uterus and round ligament. In all but four of the 10 cases there was no evidence of a connection with the uterus or tubes. In four cases a connection with the lining of these organs was strongly suggested although not absolutely proved."

According to these authors, "the etiology of this condition is unknown but in most cases the best evidence points towards transplantation or invasion (migration) of endometrium from the lining of the uterus."

This review of the literature of endometriosis in laparotomy scars shows that not only has there been definite progress toward a better comprehension of its pathogenesis, but that there is also need for further studies. It has been shown positively that scar endometriosis can arise from normally situated uterine and tubal mucosa by continuous invasion. The very strong circumstantial evidence that it also arises from the transplantation of bits of uterine mucosa in the abdominal wound during hysterotomy for the termination of early pregnancy has greatly strengthened the possibility of the transplantation and growth of this mucosa in the abdominal wound during other pelvic operations.

A large number of these cases have followed salpingectomy or tubal sterilization combined with ventrofixation of the uterus. This type of operative procedure should create conditions favorable not only for the continuous invasion of the abdominal scar by tubal or uterine mucosa, but also for the growth of bits of these mucosae transplanted in this operative field.

From the year 1926 to the present time, 17 patients with laparotomy scar endometriosis have been encountered on the Gynecological Service of the Albany Hospital. This includes four cases previously reported by the writer.[4, 7] Eleven of these patients had been operated upon primarily for conditions resulting from the injuries of childbirth: three for the sequelae of salpingitis; two for tubal pregnancy; and one for a uterine leiomyoma. In 16 patients the first operation consisted of bilateral salpingectomy or tubal sterilization followed by intentional or accidental ventrofixation of the uterus. Many of these patients

also had a preliminary uterine curettage and vaginal repair. In 10 of these 16 patients the fundus of the uterus was sutured extraperitoneally into the abdominal wound. In three patients an Olshausen type of operation, namely, ventrofixation by means of the suturing of both cornua to the abdominal wall, was performed. In all instances one or both ovaries were conserved. In one patient who had had bilateral salpingectomy for salpingitis without an inten-

Fig. 1.—Case 1. Photomicrograph (×10) of a frontal section through the left uterine cornu and a small portion of the postsalpingectomy scar endometriosis fused with it.

The patient, aged 31 years, para ii, complained of profuse and prolonged menstruation, incapacitating dysmenorrhea, and tenderness in her laparotomy scar during her menses. The latter symptom had been present for about a year. At her first operation in April, 1929, an "Olshausen ventrofixation" had been performed. "A knuckle of each tube was removed near the uterine cornu and *the raw end of the cornu was sewed against the anterior abdominal wall.*" At the second operation, March 30, 1931, the scar endometriosis together with the uterus and the right tube and ovary were removed. The uterine cavity was injected with 15 per cent melted gelatin colored with lampblack.

The mesial portion of the intramural part of the tube (the so-called "transitional zone") is well shown in this photomicrograph. At its left is the actual transition from uterine to tubal mucosa which is abrupt in this section. At its right is the lateral portion of the intramural part of the tube which forms the tubal stump. Note that gelatin, shrunken as a result of dehydration, is present in the lumen of the mesial portion of the tube and also in the glands of the mucosa lining the uterine cavity. It is even present in a gland, *a*, which has penetrated the myometrium. Only a little of the lateral portion of the intramural part of the tube appears in this section. It, too, contains gelatin, as does a lateral sprout or tubule, *b*, which has arisen from its mucosa and invaded the cornu, forming an endometriosis in this situation. Lateral sprouts originating in the mucosa of the intramural part of the tube may develop in the uterine cornua of women who have never had an operation. Even so, I believe that they may also arise from a tubal stump which has been pierced by a needle in the closing of the uterine cornu over it or as a result of the suturing of a cornu to the abdominal wall after salpingectomy, as in this case. Note the two gelatin-containing sprouts in the scar just above its fusion with the uterus. These will be discussed in the legend of the next photomicrograph.

tional suspension of the uterus, the left uterine cornu became connected with the laparotomy scar by the remains of a long persistent drainage tract. In only one patient in this series was salpingectomy not done. In this case the endometriosis followed the removal of an intramural myoma from the anterior wall of the uterine fundus. The first operation in ten of these 17 patients took place on the Gynecological Service of the Albany Hospital during the ten-year period from 1918 to 1927, inclusive, when bilateral salpingectomy or tubal sterilization, followed by ventrofixation of the uterus, had been performed 325 times. Since we have appreciated that this complication might follow this type of operation, it has rarely been employed.

The youngest patient was 28 years of age at the time of the second opera-

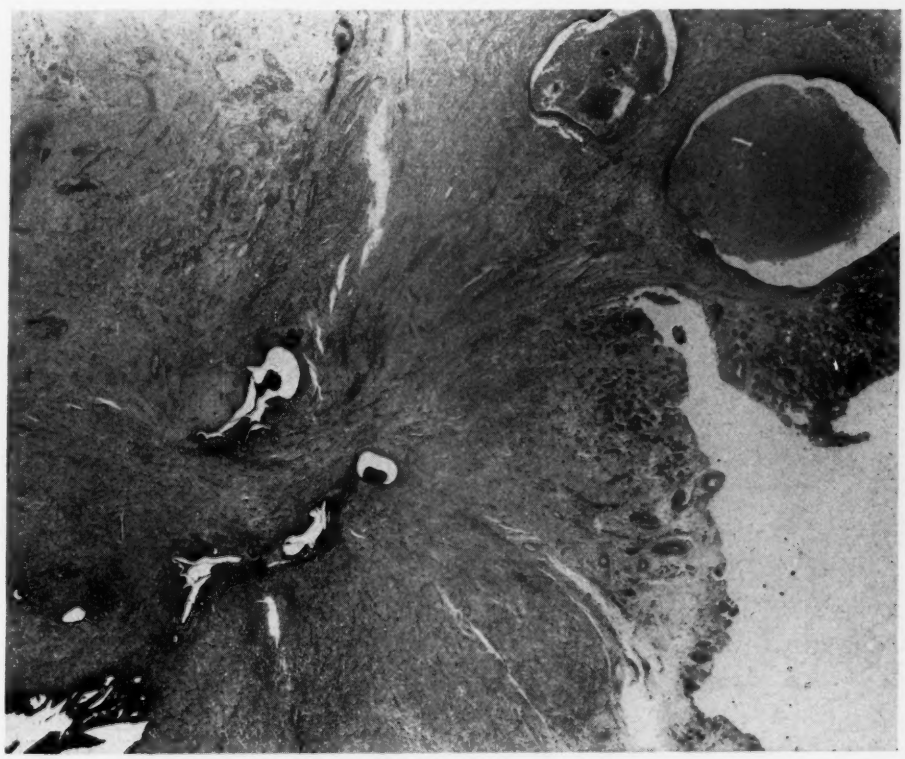

Fig. 2.—Case 1. Photomicrograph (×10) of a section similar to the preceding one and quite near it. To be more fully appreciated the two photomicrographs should be studied together. More of the scar and less of the cornu appear in this photomicrograph. Only a small part of the mesial or transitional portion of the tube and almost the entire length of the lateral portion are shown. Gelatin is present in the lumen of the lateral portion. Two gelatin-containing sprouts or tubules in the scar just above its fusion with the uterine cornu are shown in Figs. 1 and 2. The gelatin in their lumina indicates that they are continuous with the uterine cavity. From their situation one would infer that they were derived from the mucosa of the tubal stump. A study of other sections proves that the tubule at the right is definitely a terminal sprout from the mucosa of the end of the stump, while the tubule at the left appears to have been derived from a lateral sprout. The latter tubule, shown better in Fig. 1, is more definitely endometrial than the one at the right. Two large dilated tubules or cavities, lined by columnar epithelium and filled with old blood, are situated in the upper right portion of this section. A study of these two cavities in other sections suggests that they were probably derived from the two sprouts just described.

tion, and the oldest, 47 years; three were over forty. The shortest interval between the two operations was two years and the longest, seventeen. Symptoms referable to the scar endometriosis appeared in the majority of these patients in from one to three years after the first operation. However, two patients with extensive endometriosis did not have any symptoms referable to it until fifteen and sixteen years, respectively, after the first operation.

The pathogenesis of postsalpingectomy and posttubal sterilization endometriosis in lapartotomy scars is but a further chapter in the complications resulting from the repair of salpingectomy wounds. In a previous study by the writer,[7] tubal stumps from 100 patients who had had previous salpingectomy or tubal sterilization were carefully examined microscopically, many after injecting the uterine cavity with colored gelatin. As bilateral salpingectomy or

Fig. 3.—Case 1. Photomicrograph (×10) of a section from a part of the same block as the two preceding ones. Only a small portion of the cornu is shown. The scar endometriosis evidently had been torn in excising it. The tubular sprouts appearing in the two previous sections have invaded the scar more deeply. Gelatin is present in the tubules below the tear. A study of other sections from this general region strongly suggests that the endometriosis above the tear was continuous with that below it. The latter was derived from the mucosa of the tubal stump by continuous invasion. All the Müllerian mucosa in this portion of the scar endometriosis is definitely uterine in type. Yet the evidence is that this typical uterine mucosal tissue developed in the sprouts or tubules which grew out from the mucosa of the lateral portion of the intramural part of the tube. Was this portion of the tube lined by tubal or uterine mucosa? If the former, it must have been potentially endometrial. If the latter, it was abnormal for this portion of the intramural part of the tube. It is my belief that the endometrial type of tissue in the scar endometriosis actually arose from tubal mucosa which was potentially endometrial.

tubal sterilization had been done in 47 patients, a total of 147 stumps was available. Misplaced Müllerian mucosa was found in or about 112 stumps as compared with 16 instances of misplaced Müllerian mucosa in 200 cornua from 100 uteri, with intact tubes. Even in 50 uteri with intact tubes removed for the sequelae of salpingitis (a well-recognized cause of cornual endosalpingiosis), misplaced Müllerian mucosa was found in only 19 of the 100 uterine cornua. Therefore, preoperative endometriosis must be present in only a relatively small percentage of patients with tubal stumps. Postsalpingectomy endometriosis is but an evidence of the results of overactivity on the part of the tubal mucosa in the repair of salpingectomy wounds. It manifests itself by the outgrowth of sprouts, terminal or lateral, which arise from the mucosa of the tubal stump. These outgrowths in the form of tubules may invade not only the tissues about the stump, such as the uterine cornu in which the stump is frequently buried, but also any structure or organ such as intestine, ovary, or even the abdominal wall which may become adherent to this operative field.

Fig. 4.—Case 2. Frontal section through the fundus uteri and the postsalpingectomy scar endometriosis fused with the left cornu (×¾).

The patient, aged 37 years, para i, complained of severe dysmenorrhea and soreness in her laparotomy scar for the previous two years. This soreness was much greater during menstruation. She had been operated upon June 1, 1927, for prolapse of the uterus. At that time the uterus was curetted, the cervix amputated, pelvic floor repaired, appendix removed, both tubes severed close to the uterus and their cut ends buried in the cornua. The fundus of the uterus was then sutured extraperitoneally in the abdominal incision. At the second operation, Oct. 9, 1930, the scar endometriosis, which was fused with the left uterine cornu, was removed together with the uterus and both tubes and ovaries.

While distending the uterine cavity with gelatin colored with lampblack, some of the injection mass escaped from the left side of the scar endometriosis (see arrow). This phenomenon demonstrated that some of the endometriosis had been injured and possibly not removed. However, it was of much greater interest to me that Müllerian tubules and cavities in the scar must have been continuous with the uterine cavity. Endometriosis was present in both uterine cornua, but that in the right cornu, which arose from the mucosa of the distal stump of the tubal sterilization, had not invaded the laparotomy scar. A second and much smaller focus of endometriosis was present just below the first one in the subcutaneous portion of the scar. It was not adherent to the fundus of the uterus. It could have originated either as a part of the larger focus or as an independent process of transplantation origin.

One of the most interesting features of this misplaced Müllerian mucosa is that it may present both the structure and function of the uterine mucosa. This phenomenon may even occur in endometriosis arising from the mucosa of stumps of the isthmus of the tube. The tubal stumps in postsalpingectomy scar endometriosis have been situated in the intramural part of the tube in all the specimens which I have studied. Excellent descriptions of this part of the tube appear in papers by Schneider[11] and also by Geist and Goldberger.[12]

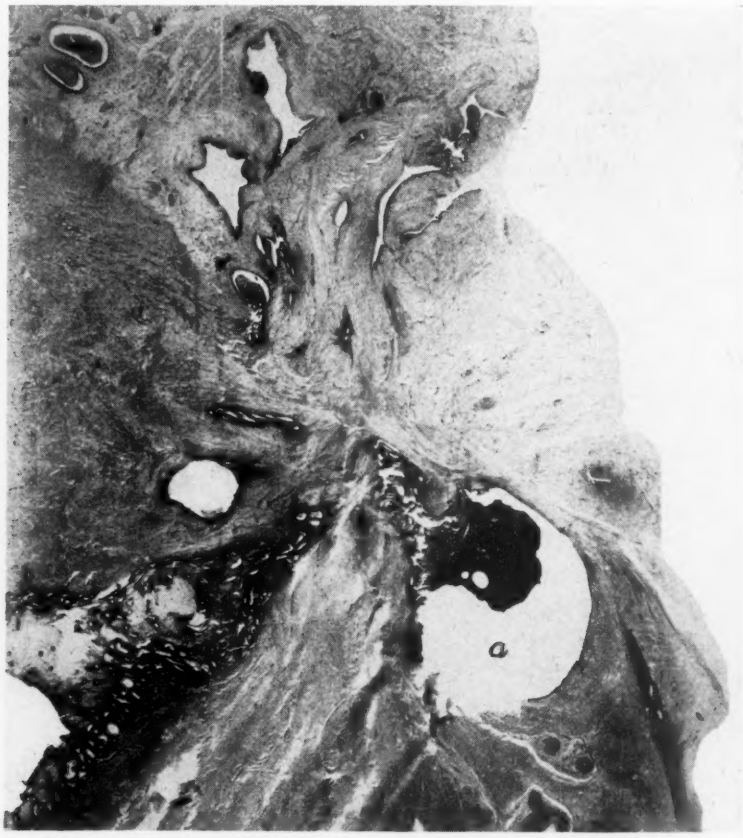

Fig. 5.—Case 2. Photomicrograph (×5) of a frontal section of the left uterine cornu and a portion of the scar endometriosis fused with it. A small portion of the uterine cavity and nearly all of the intramural part of the tube appear in this section. The intramural portion of the tube is lined by uterine mucosa and constitutes the tubal stump since the tube was severed close to the cornu. Shrunken bits of gelatin are present in the lumina of many of its endometrial glands. A magnifying glass is of great assistance in detecting the finer details of this tissue. To the right of the stump is an oval cavity, *a*, partially filled with the injection mass. It could be a distended portion of a tubule. Typical uterine mucosa with gelatin in the lumina of many of its glands occupies the upper portion of this cavity. This mucosa is continuous with similar mucosa in the cornu above and to the left of cavity *a*. To the left of this and above the end of the stump, is a narrow strip of uterine mucosa also with gelatin in the lumina of its glands. Other sections from this same general region demonstrate that these two ectopic foci of uterine mucosa with gelatin in their glands are continuous with each other and with the mucosa of the tubal stump. Therefore, they must have been derived from the latter by continuous invasion. In this section there is no indication of a continuity between the cornual endometriosis and that in the scar.

During the study of tubal stumps, endometriosis, which can be shown not to be continuous with the mucosa of the stump, is sometimes found in the operative field of the salpingectomy. Experimental salpingectomy was performed on uteri after their removal, in some of which the stump was purposely transfixed by a needle carrying a suture or otherwise traumatized. Microscopic studies of 48 of these uterine cornua showed bits of tubal mucosa embedded in 16 of them. If bits of tubal mucosa transplanted during salpingectomy grow in the immediate operative field, they should also sometimes grow in more remote fields, including the abdominal wound.

Frequently, a preliminary uterine curettage is done prior to a salpingectomy or tubal sterilization. During the manipulation of the uterus incident to

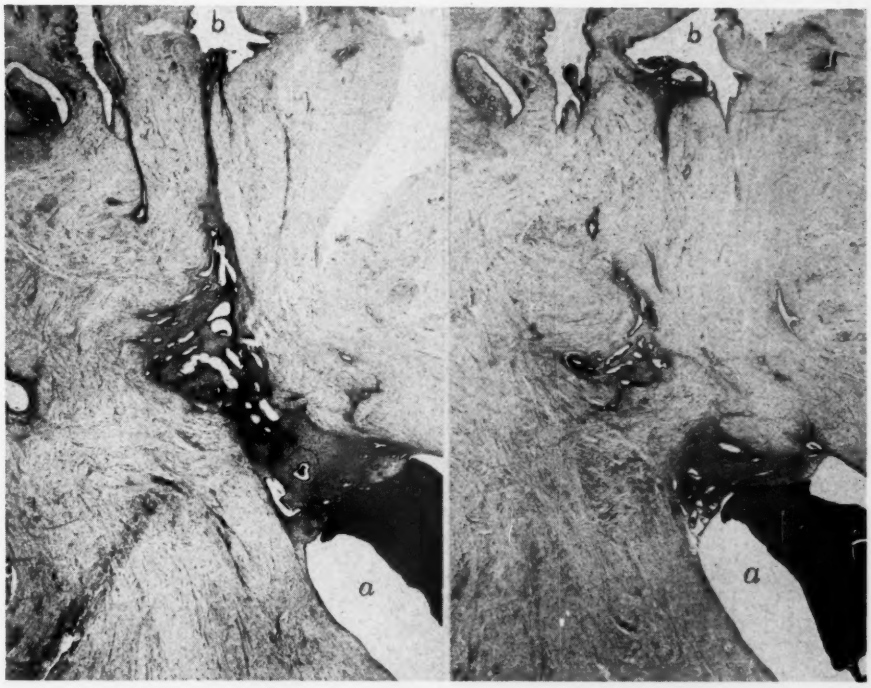

Fig. 6.—Case 2. Photomicrographs (×8) of two sections cut from the same block as the section shown in Fig. 5. These two photomicrographs should be studied together. The tubal stump no longer appears in either of these sections. However, the cavity labeled *a* is still present. It is lined by columnar epithelium which is continuous with that covering the endometrium in the upper portion of the cavity and also with that lining the glands which open on its surface. This uterine mucosa is likewise continuous with similar mucosa in the uterine cornu above cavity *a*. The latter mucosa has invaded the scar and appears to have invaded a small endometrial cavity or cyst, *b* (probably a dilated tubule). In the second section the lumina of some of the glands of the mucosa of this cavity contain gelatin, which can readily be detected with the help of a magnifying glass. This mucosa was derived from endometriosis in the cornu and the latter arose from the mucosa of the tubal stump, all by continuous invasion. The gelatin in these glands was injected into the uterine cavity and permeated their lumina as though they were lymph vessels. The presence of the injection mass in the lumina of these glands in the endometriosis of the cornu and the scar indicates that they are continuous with each other and with the lumen of the tubal stump and through it with the uterine cavity. The epithelium lining these glands is, therefore, continuous with that of the mucosa of the tubal stump and, through the latter, with the epithelium lining the uterine cavity.

Fig. 7.—Case 3. Photomicrograph (×5) of a frontal section through a postsalpingectomy scar endometriosis and a portion of the left uterine cornu fused with it.

The patient, aged 34 years, para ii, complained of pain in her laparotomy scar, worse after the cessation of her menstrual flow. She had been operated upon Sept. 11, 1926, for an adherent retroflexed uterus associated with a relaxed pelvic floor. The uterus was curetted, cervix amputated, and pelvic floor repaired. The left tube and ovary and the right tube were removed and the fundus of the uterus sutured extraperitoneally in the abdominal incision. The second operation was performed Sept. 21, 1932, when the uterus, together with the scar endometriosis fused with its left cornu, was removed.

The scar endometriosis contains many tubules, some small, others large. Some are lined entirely by columnar epithelium, others partly by epithelium and partly by uterine mucosa. Gelatin (shrunken as a result of dehydration) is present in many of them. Note especially the dilated tubule *a* and beneath it several smaller tubules (possibly all sections of the same tubule) each containing gelatin. The lumina of other tubules appear to be empty although some of the larger ones contain old blood. What is the origin of these tubules? I believe they arose as sprouts from the mucosal epithelium of the uterine cornu, shown at the left margin of the photomicrograph. This mucosa is in reality the mesial portion of the intramural part of the left tube and actually constitutes the tubal stump since the lateral portion of this part of the tube was excised by me at the first operation. Note that gelatin is present in the lumina of glands of the mucosa of the stump. Also note the small gelatin-containing tubule just above and to the right of the stump and its suggested continuity with the string of small tubules beneath dilated tubule *a*. The manner in which the tubules of the scar endometriosis arose from the mucosa of the tubal stump is shown in Fig. 8.

Fig. 8.—Case 3. Photomicrograph (×5) of a section from the same block as the preceding one and quite near it in the series.

The enlarged, distorted tubule marked *b* in Fig. 7, partially lined by uterine mucosa, including a polyp, appears in this section as two tubules separated by scar tissue. The dilated tubule *a* is smaller in this section than in the preceding one and a focus of uterine mucosa is present within it. Compare this with tubule *b* in Fig. 6 and note their great similarity. Note also the tubules beneath it which follow a course similar to those beneath tubule *a* in the preceding section. Like those, they are probably sections of the same tubule, the "stepping-stone" arrangement of which suggests that its course is very tortuous. Observe, too, the changes in the tubal stump. Its glandular tissue is now much nearer the scar than in the preceding section, is more distorted, larger, and more spread out, due to the fact that at least three sprouts have taken origin from it and invaded the uterine cornu about it. All of the gelatin-containing tubules shown in these two sections are not only continuous with each other but also with the glands in the mucosa of the tubal stump and through them with the uterine cavity. The continuity of all these lumina is clearly demonstrated by the presence of gelatin within them. The gelatin found its way out of the uterine cavity through tubules which arose from the mucosa of the tubal stump. *Tubules have, therefore, played just as important a role in the pathogenesis of the scar endometriosis in this case as glands did in the previous one.* What is the difference between Müllerian tubules and glands? Compare carefully the photomicrographs in the two cases. In the one case Müllerian tubules clothed in stroma formed the major part of the invading tissue; in the other, Müllerian tubules without appreciable stroma about them.

the salpingectomy, blood carrying bits of the uterine mucosa may escape through the uterine end of the severed tube (see Fig. 4 in previous paper[4]) and may be transplanted not only in the uterine cornu, but even in the peritoneal cavity or in the abdominal wound. Transplanted Müllerian mucosa has been held by many writers to be responsible for some of the endometriosis in laparotomy scars which followed salpingectomies.

The indications for the second operation varied greatly. The discomfort from the scar endometriosis was an important presenting symptom in 14 pa-

Fig. 9.—Case 4. Postsalpingectomy endometriosis of a laparotomy scar adherent to the left uterine cornu of a multinodular myomatous uterus (×¾).

The patient, aged 37 years and nulliparous, complained of profuse menses and severe dysmenorrhea during the previous two years. For the past year she also had had severe pain in the scar during menses, often associated with a discharge of blood from it at that time. The first operation occurred in the year 1920 when the appendix, both tubes and the left ovary were removed for "salpingitis" and both uterine cornua were sutured to the abdominal wall. At the second operation, July 10, 1936, the scar endometriosis together with the uterus and right ovary were removed.

Multiple uterine myomas and endometriosis in both uterine cornua are present. The endometriosis in the right cornu is confined to the uterus. It apparently arose from two sources, namely, the uterine mucosa of the cornu and the tubal mucosa of the stump. That which arose from the mucosa of the cornu is mainly uterine in type and that from the mucosa of the stump is tubal in type. The endometriosis in the left cornu is almost entirely of tubal type and is continuous with the endometriosis in the scar above and adherent to it. Note that symptoms referable to the scar endometriosis did not appear until nearly fifteen years after the first operation.

tients. Two of these had a bloody drainage from the scar during menstruation. Three of the patients also had uterine leiomyomas which caused menstrual disturbances. Symptoms referable to the scar endometriosis were pain and tenderness in the scar during menstruation which in some instances persisted after the cessation of the flow. The endometriosis was without symptoms in only two patients.

At the second operation the entire uterus, together with the portion of the laparotomy scar containing the endometriosis which was fused with or otherwise attached to the fundus uteri, was removed intact in 15 patients. In one patient who had had both tubes, one ovary, and a myoma removed twelve years before, a very extensive endometriosis of the abdominal wall developed, so massive that only a portion of it and the remaining ovary were removed.

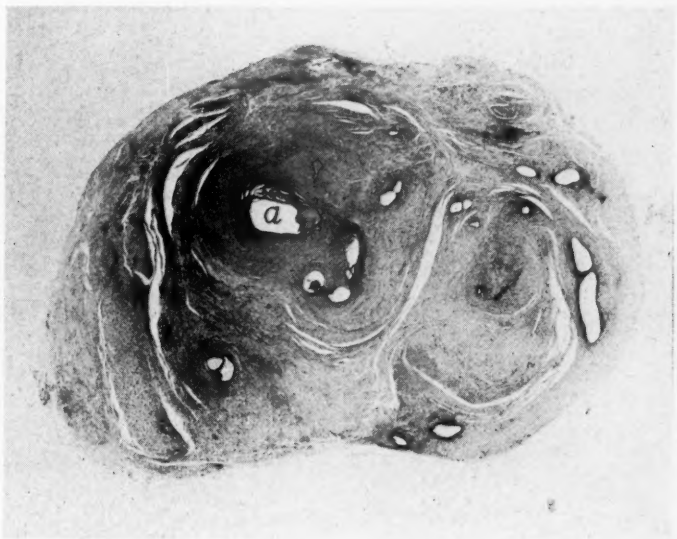

Fig. 10.—Case 4. Photomicrograph (×5) of a horizontal section of the left uterine cornu, just below its attachment to the abdominal wall as shown in the preceding illustration. A cross section of the lumen of the mesial portion of the intramural part of the tube, which constitutes the tubal stump, appears at *a*. The lumen is partially lined by uterine mucosa and contains gelatin. Gelatin is also present in the tubule beneath it. The origin of this tubule, as a lateral sprout from the mucosa of the tube, can be seen in preceding sections, and in succeeding sections it can be shown that nearly normal healing of the end of the salpingectomy stump has occurred. Ectopic uterine mucosa does not appear in this section. The epithelial proliferation is all of tubal type, namely, endosalpingiosis, although the mucosa of the tubal stump from which it arose is partly lined by uterine mucosa. The injection of the tubules in this section is incomplete.

The specimens removed at operation were studied in the following manner: In 12 of them the uterine cavity was injected through the cervix with 15 per cent melted gelatin colored with some pigment, as in previous studies of the repair of tubal stumps. Lamp black proved to be very satisfactory. The remainder were not injected. Then the entire specimen, usually without incising the uterus, was chilled in ice water and hardened in 10 per cent formalin. Before or after fixation, sketches were made of it for future reference. The

"blocks" were so made that sections of the scar endometriosis and the portion of the uterus fused with it would show not only the relation between the ectopic Müllerian mucosa in the scar and any in the uterine wall, but likewise the origin of the latter from either the mucosa of the tubal stump or that of the uterus. The blocks were embedded in celloidin and many sections were cut.

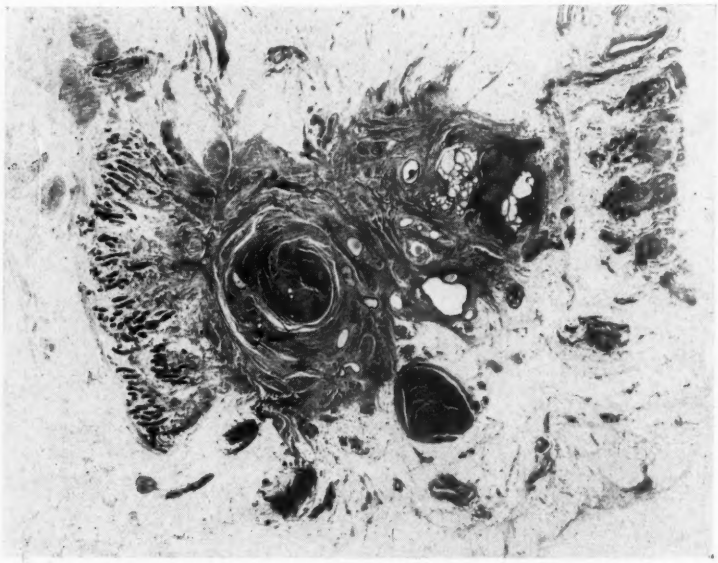

Fig. 11.—Case 4. Photomicrograph (×5) of a cross section of the scar endometriosis including some of the left rectus muscle. This section is taken about halfway between the section shown in the preceding illustration and the following one, and from the same series. Many tubules of varying sizes appear in cross section. Gelatin is evident in the lumina of only a few of these. However, its presence establishes the continuity of the lumina of these tubules with that of the intramural portion of the tube and through it with the uterine cavity. Uterine mucosa does not appear in the scar endometriosis in this section. It is occasionally encountered in some sections intermediate between this and those shown in the preceding and following figures. In these sections, however, the uterine mucosal tissue is relatively insignificant compared with that shown in Fig. 12.

Sections from many levels were always studied and in some situations serial sections were prepared. Even in noninjected specimens one may sometimes obtain a fairly accurate conception of the pathogenesis of the scar endometriosis. When one finds endometriosis of the uterine cornu which can be seen to have arisen from the mucosa of the tubal stump and when similar endometriosis is present in the scar fused with that cornu, the endometriosis in the two situations appearing to be continuous, one may justifiably conclude that the endometriosis in the scar probably is derived from the mucosa of the tubal stump by continuous invasion. In a specimen in which gelatin has been injected into the uterine cavity, if gelatin is detected in the lumina of tubules and other Müllerian cavities of a scar endometriosis, we have positive proof that these misplaced Müllerian cavities are continuous with the uterine cavity. The same telltale gelatin may enable one to ascertain the exact source of the scar endometriosis and the route taken by its mucosa in reaching the scar.

An example of the great value of this method of study was shown in a case of scar endometriosis in which the fundus uteri was not in actual contact with the abdominal wall at the close of the original operation but became connected with it by the remains of a drainage tract 7 cm. long. Gelatin injected through the uterine cavity was found in the scar endometriosis and also in endometriosis about the left tubal stump and in the entire length of the remains of the drainage tract. The latter was lined by columnar epithelium derived from the mucosa of the tubal stump. (See Case 5.)

In eight of the 12 specimens in which gelatin had been injected into the uterine cavity, gelatin was found in the lumina of some of the tubules and other ectopic Müllerian cavities of the scar endometriosis and also in the endometriosis about the end of the tubal stump. The exact source of the scar endometriosis in these cases was more easily and more convincingly demonstrated than in the specimens which had not been injected. In all of the eight specimens the scar

Fig. 12.—Case 4. Photomicrograph (×5) of a section of a portion of the scar endometriosis including the skin and subcutaneous tissues of the scar shown in Fig. 9 cut in a plane at a right angle to the preceding sections. Note the change in the Müllerian tissue. While tubules are present as in the preceding section, typical uterine mucosa is also present. There seems to be a very intimate relation between these two types of Müllerian structures as though typical uterine mucosa had arisen from the lining of the tubules. Gelatin is not found in the lumina of any of the tubules or of the glands of the uterine mucosa in this portion of the scar endometriosis. However, it is present in the lumina of tubules in sections from a block of the subcutaneous portion of the scar endometriosis adjacent to this one. In these sections very little mucosa of uterine type is seen.

The "spotted" injection of the lumina of tubules in scar endometriosis has its significance but is most tantalizing and also stimulating. What is the source of the typical uterine mucosa in this section? I believe that all of the Müllerian epithelium came from the mucosa of the tubules in the preceding sections, beginning with the one shown in Fig. 10. The source of the stroma, however, is more difficult to determine and presents an interesting problem.

endometriosis arose from the invasion of the abdominal wall by the mucosa of the tubal stump.

In each of the scars of two of these eight specimens, two distinct and separate foci of endometriosis were present. In the first case endometriosis had developed about each uterine cornu. In the tubular structures of one focus gelatin was found but it was not present in the other. The origin of the first focus was undoubtedly due to tubules from the mucosa of the end of the tubal stump which had invaded the tissues of the abdominal wall about the stump. In the second focus the endometriosis could have been of transplantation origin (see Case 2 in a previous paper[7]). The second case with two separate foci was

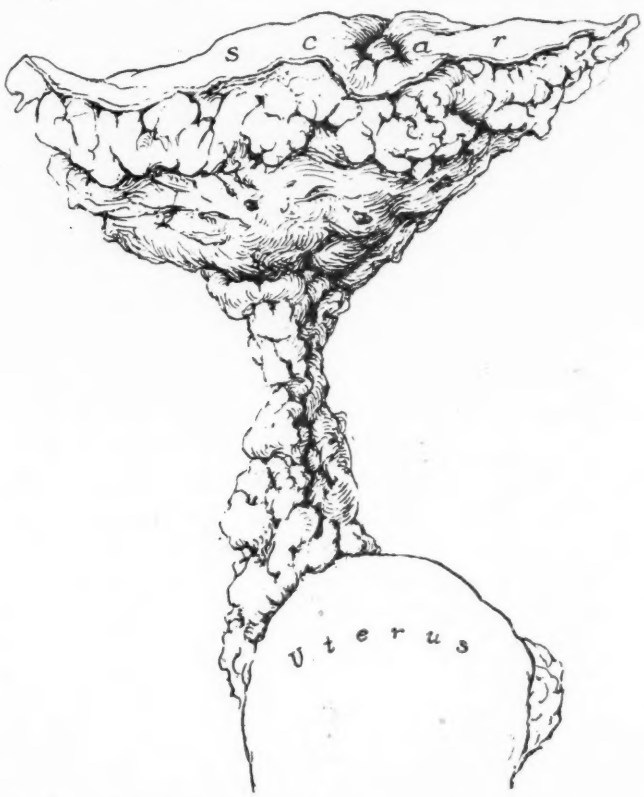

Fig. 13.—Case 5. Postsalpingectomy endometriosis of a laparotomy scar attached to the left uterine cornu by a drainage tract 7 cm. long (×¾).

The patient, aged 34 years, para iii, complained of severe pain in her laparotomy scar, especially during menstruation. She had first been operated upon on Feb. 21, 1938, when the appendix, both tubes, and the left ovary were removed for bilateral subacute salpingitis. The pelvis was drained through the abdominal incision by rubber tubes which were removed on the tenth postoperative day. A persistent drainage tract resulted which would "close and reopen with a bloody discharge at every menstrual period since the first one, ten weeks after the operation." At the second operation, Oct. 3, 1940, the scar endometriosis together with the uterus, right ovary, and remains of the long drainage tract were removed.

The uterine cavity was distended with lampblack-colored gelatin which was later found in the lumina of some of the tubules and cavities in the base of the scar endometriosis, thus demonstrating their continuity with the lumen of the drainage tract and through it with the tubal stump and the uterine cavity.

similar to the one just described in that gelatin was found in the scar endometriosis which was fused with one uterine cornu. It was not found, however, in the second focus which had no apparent connection with either the first focus or with the fundus of the uterus. The second focus of scar endometriosis could have been of transplantation origin.

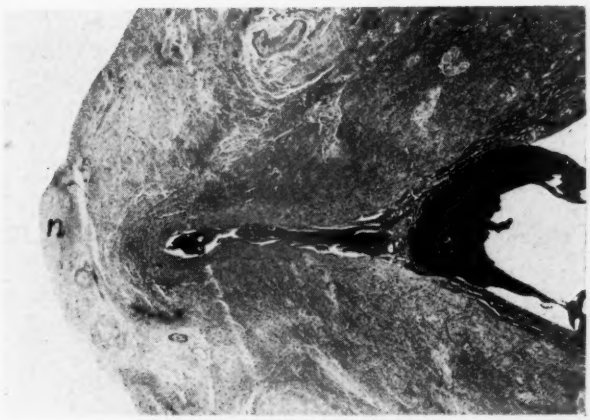

Fig. 14.—Case 5. Photomicrograph (×5) of a horizontal section of the right uterine cornu shown in Fig. 13. Some of the uterine cavity, all of the mesial and the beginning of the lateral portion of the intramural part of the tube, appear in this section. The remainder of the lateral portion appears in succeeding sections of this series, in which it is shown to end without either terminal or lateral sprouts in the small nubbin marked *n*. The transition between uterine and tubal mucosa occurs quite abruptly at the beginning of the mesial portion of the intramural part of the tube.

The absence of gelatin in the lumina of Müllerian tissue in a scar endometriosis does not always signify that the ectopic tissue had not arisen by continuous invasion from the mucosa of a tubal stump. When gelatin was found in the lumina of this tissue, it was usually in the lumina of tubules in the base of the scar endometriosis near the tubal stump. In only one of the eight specimens in which gelatin was found in the lumina of the tubules was it present in all parts of the scar endometriosis. Even in this case, however, it was not present in every tubule. (See Case 3.) Nevertheless, some of the most interesting observations were made in specimens with a limited injection of the scar endometriosis. (See Case 2.) The failure to obtain more complete injections must have been due either to actual obstruction of the lumina of the tubules which were partially injected or not injected at all, or to the employment of insufficient pressure when injecting the gelatin mass through the uterine cavity. Uterine mucosa frequently develops in the lining of these tubules. I am sure that this phenomenon was responsible for the failure, in at least some instances, of the injection mass to penetrate the endometriosis more extensively. I tried using greater pressure during the injection of the uterine cavity but this procedure only caused the extravasation of gelatin into the interstitial tissues of the endometrium, especially in the ectopic uterine mucosa.

We know that the intramural portion of the tube may be occluded in patients who have never been operated upon and may, therefore, be present be-

fore the first operation is performed. Such occlusion may also develop after the first operation, proximal to the incised end of the tubal stump and may have no relation to it. In these cases gelatin could not pass from the uterine cavity into any tubules which might arise from the end of the stump. Under these circumstances gelatin would not be found in the tubules of the scar endometriosis. Gelatin also would not be present in the tubules of a scar endometriosis of transplantation origin or in one resulting from the extension of a peritoneal endometriosis of the portion of the uterine fundus which became adherent to the scar.

In four of the 12 injected uteri, gelatin was not found in the scar endometriosis. In the first of these the scar was fused with the central portion of the

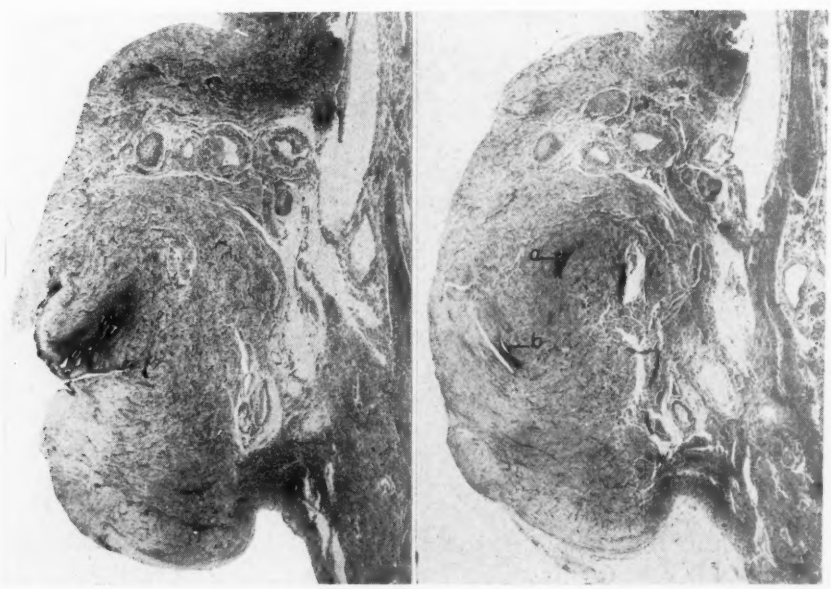

Fig. 15.—Case 5. Photomicrographs (×8) of two sections of the nubbin marked *n* in the preceding illustration and from the same series.

In the first section the endometriosis consists of glands and stroma similar to uterine mucosa. Mesial sections in the series show that, at present, this mucosa is not continuous with the mucosa of the tubal stump but is situated very near the end of the stump. The second photomierograph is also of the same nubbin in a nearby mesial section. Here lampblack appears in a lumen *a* which resembles that of the isthmus of the tube but lacks an epithelial lining. However, mesial section show lumina continuous with this one, which contain lampblack and are lined by normal-appearing tubal mucosa. Below the end of the tubal stump *a* is a narrow space *b* lined by Müllerian-like tissue including its epithelium, but without lampblack in its lumen. This tissue is not continuous, now, with tubal mucosa mesial to it but is a part of the endometriosis shown in the first section.

This series of sections of the uterine cornu portrays the operative technique probably employed in removing the tube from the uterine cornu. They also show some of the results of the attempted repair of the damage (mutilation) inflicted upon the tubal stump during the operation, such as severing the tube, possibly clamping it, and, in this instance, strangulation by sutures. I believe that the endometriosis shown in the first photomicrograph arose from a bit of tubal mucosa which was "pinched off" or otherwise separated from the rest of the stump during the operation. A tightly tied suture could have done this very readily. I also believe that this bit of mucosa was *originally of tubal type and has acquired the structure of uterine mucosa.*

uterine fundus and the endometriosis was believed to have been derived from the mucosa lining the uterine cavity and not from the mucosa of a tubal stump.

In the second case, small foci of endometriosis were present in the scar fused with the right uterine cornu and also about the ends of the tubal stumps in both cornua. Gelatin was present in the lumina of both tubal stumps but not in the endometriosis about them or in the scar. This could have been caused by the occlusion of the lumina of the ends of the tubal stumps after development of the scar endometriosis.

The third case in which no gelatin was found in the endometriosis of the scar was most confusing. It presented the appearance of an endometriosis arising on the surface of the cornu and simultaneously invading the myometrium beneath it and the adjacent scar which was fused with the uterine wall. Peritoneal endometriosis, however, was not observed at the time of the first operation. Microscopic examination of the tissues about the tubal stump in this case was unsatisfactory.

Fig. 16.—Case 5. Photomicrograph (×5) of a horizontal section of the left uterine cornu and the scar fused with it at the base of the drainage tract shown in Fig. 13 and approximately at the same level as the section of the opposite cornu shown in Fig. 14. Nearly the entire intramural part of the tube is shown in this section. It constitutes the tubal stump because the tube had been removed close to the cornu. It is lined by typical uterine mucosa with gelatin in the lumina of its glands. The extravasation of gelatin into the distal portion of this mucosa marred this tissue and also permitted the escape of more gelatin into the drainage tract than otherwise would have occurred. However, in spite of this artefact, it is clear that the columnar epithelium lining the drainage tract was derived from the stump mucosa which had invaded its lumen before the uterus was removed. (See the next photomicrograph.)

There is a postoperative endometriosis in the scar, at the right, which is fused with the uterine cornu. Gelatin is present in its Müllerian tubules. These tubules arose as lateral sprouts from the mucosa of the stump and invaded the scar as laparotomy scars are invaded under similar conditions. (Compare with a similar section of the right cornu shown in Fig. 14.) Both cornua had the same operative treatment except that a persistent drainage tract was in contact with the left uterine cornu and not with the right. The entire intramural part of the right tube is lined with tubal mucosa while that of the left is lined with uterine mucosa. Direct endometriosis has arisen from the mucosa of the left tubal stump but not from that of the right stump.

Fig. 17.—Case 5. Photomicrograph (×5) of a section of the uterine cornu and scar endometriosis shown in the preceding illustration, and from the same series, about 5 mm. above the latter.

Gelatin is present in the tubules and also in the larger "cavity" of the scar. This cavity is merely a cross section of the lumen of the lower portion of the former pelvic drainage tract which had extended through the abdominal incision. It is lined by columnar epithelium except for typical uterine mucosa which occupies the portion of the "cavity" nearest the uterine cornu. The sections between the preceding illustration and this one demonstrate that the uterine mucosa shown here is continuous with that of the stump and that the latter has grown out through the end of the stump into the lumen of the tract. The columnar epithelium lining the tract must have been derived from this mucosa.

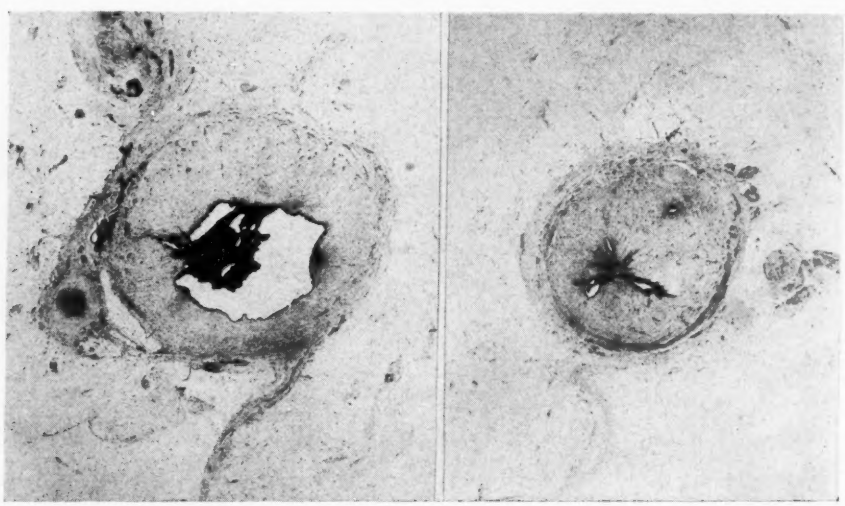

Fig. 18.—Case 5. Photomicrographs (×5) of two cross sections, taken at different levels, of the drainage tract shown in the preceding illustration. The first is from the lower portion of the tract above the last section and the second is from the upper portion, just below the section shown in the next illustration. The entire tract is lined by columnar epithelium which is continuous with the epithelium of the mucosa of the tubal stump and also with that of the Müllerian structures in the scar endometriosis. The second section is from the narrowest portion of the tract.

In the fourth and last case, a preliminary uterine curettage, removal of the right tube and ovary for tubal pregnancy, and left tubal sterilization followed by ventrofixation of the uterus had been performed. The second operation, seventeen years later, was undertaken for dysmenorrhea and too frequent menstruation associated with pain and tenderness in the abdominal scar. The latter symptoms had been noticed for only a year. At the second operation, the scar endometriosis, fused with the right uterine cornu, was removed with the uterus. A small focus of endometriosis was found about the end of the tubal stump in each cornu. The endometrial tissue in the right cornu arose from the mucosa of the tubal stump and its tubules contained gelatin. A careful study of this cornu and the portion of the scar adherent to it failed to show any connection between the endometriosis of the cornu and that in the scar. It was judged that the scar endometriosis might have resulted from the transplantation of endometrial tissue. The preliminary uterine curettage at the first operation increased the possibility of such an origin.

In four of the 16 specimens from patients with bilateral salpingectomy or tubal sterilization, the uterine cavities were not injected. Two of the patients were operated upon before the method was employed. In both of these cases

Fig. 19.—Case 5. Photomicrograph (×2½) of a cross section through the central portion of the scar endometriosis shown in Fig. 13, and at a right angle to the preceding sections of the drainage tract. This section also includes the terminal portion of the intra-abdominal part of the drainage tract at the left and the skin covering the scar at the right. The portion of the tract shown here has again a relatively large lumen which becomes much smaller at the point, not shown in this illustration, where the tract enters the base of the scar. In the latter location many tubules arise from the tract and invade the scar in as many directions. As previously stated, the entire tract is lined by columnar epithelium continuous with that of the mucosa of the tubal stump. However, other sections in this series show that uterine mucosa, sometimes in polypoid form, has in places replaced the lining of the more proximal portion of the tract. Gelatin was found in the lumina of several tubules and even in the glands of typical uterine mucosa in the base of the scar endometriosis (not shown). One may thus conclude that at least all of these tubular structures were continuous with the lumen of the drainage tract and through it with the uterine cavity.

There is only one possible source of the Müllerian mucosa in this scar endometriosis, namely, the lining of the drainage tract, and the latter came from the mucosa of the tubal stump, all by continuous extension and invasion.

the scar endometriosis was fused with a uterine cornu in which endometriosis was present. These two cases have been previously reported[4] and also mentioned in the present paper.

In a third case, the second operation was performed thirteen years after the previous one in which a myoma, both tubes, and one ovary had been removed, and both uterine cornua sutured to the abdominal wall. The scar endometriosis, fused with both uterine cornua, was so extensive that only a portion of it and the remaining ovary were removed.

In the fourth case, the last operation was performed ten years after the previous one. The scar and the fundus uteri were so badly mutilated in removing them that the uterine cavity was not injected. The portion of the scar adherent to the left uterine cornu contained a hemorrhagic cyst, 3.5 cm. in diameter and partially lined by columnar epithelium. Müllerian tubules were present both in the uterine cornu about the stump and in the fibrous tissue uniting the cornu with the tissue about the cyst. One would infer that the scar endometriosis was derived from the mucosa of the tubal stump by continuous invasion or transplantation.

Discussion

Seventeen cases of laparotomy scar endometriosis have been studied. The first operation, in all but one case, consisted of bilateral salpingectomy or tubal sterilization followed by intentional or accidental ventrofixation of the uterus. In the one case in which salpingectomy had not been done, the scar endometriosis followed a myomectomy. In all but one of the 16 postsalpingectomy cases, the scar, together with the uterus, was removed at the second operation. In that one case the endometriosis, apparently fused with both uterine cornua, was so extensive that only a portion of it and the remaining ovary were removed. In all but two of these 15 specimens the scar endometriosis was fused with a uterine cornu. In one of these two cases the fundus was not in actual contact with the wound at the close of the first operation but its left cornu became connected with the scar by the remains of a long drainage tract. In the other case the scar endometriosis was fused with the center of the fundus and not with either uterine cornu although stump endometriosis was present in both. In this case I believe that the scar endometriosis was derived from the mucosa of the fundus by continuous invasion in the attempted repair of an evident rent in the uterine wall, probably caused by a ventrofixation suture which had penetrated the uterine cavity.

Endometriosis was found about the tubal stumps in the 13 uterine cornua which were adherent to the scar endometriosis as well as in the cornu not in actual contact with the scar but connected with it by a long drainage tract. It was present about the tubal stumps in both cornua in 11 of these 14 uteri but in only one instance had the endometriosis in both cornua invaded the scar, thus causing two foci of endometriosis in it. In the remaining 10 cases, the scar endometriosis was derived from only one tubal stump and that about the other stump was confined to the cornu itself.

I was able to ascertain that the scar endometriosis was derived from the mucosa of a tubal stump by continuous invasion in 10 specimens. It probably arose in a similar manner in three others. In two additional specimens such an origin could not be excluded although one of these might have been of transplantation origin and the other secondary to a possible peritoneal endometriosis of the uterine cornu.

Transplantation endometriosis was possibly present in three scars. One of these is mentioned above. In the remaining two cases two separate foci of endometriosis were found in each scar, one of which was proved to have arisen by continuous invasion from the mucosa of a stump. The other possibly developed as a result of transplantation.

The postsalpingectomy scar endometriosis which I have studied has resulted from the outgrowth of terminal or lateral sprouts of the mucosa of the tubal stump. These, as tubules, invade the tissues about the stump, usually the uterine cornu. From here they spread to the portion of the laparotomy scar attached to that cornu.

Injecting the uterine cavity with colored gelatin, a method proved to be of great value in studying the pathogenesis of postsalpingectomy endometriosis in other situations, has also been very helpful in the study of these cases, in 12 of which the uterine cavity was injected. Gelatin was found in the scar endometriosis in eight of these, thus demonstrating the continuity of their tubules with the uterine cavity. The same "telltale" gelatin indicated the source of the endometriosis and the routes taken by sprouts from normally situated Müllerian mucosa in their invasion of the scar. The most dramatic demonstration of the great value of the injection method in ascertaining the pathogenesis of postsalpingectomy scar endometriosis was the presence of gelatin in the tubules of a scar in which the only contact with the uterus was the remains of a drainage tract 7 cm. long. This same specimen likewise showed the ability of Müllerian tissue to extend itself by continuous growth and invasion for a long distance. In this instance the mucosa of the left tubal stump had grown out through the end of the stump into the lumen of the drainage tract entirely lining it with columnar epithelium. The drainage tract ended, as such, at the base of the scar. Here sprouts had arisen from its mucosa and had invaded the scar actually to the skin epithelium. The total distance traveled by the continuous extension and invasion from the stump mucosa was 11 centimeters. (See Case 5.)

In four of the 12 injected specimens, the gelatin did not reach the scar endometriosis. The reason for this failure was judged to be a mechanical one in three instances and actual lack of continuity in the fourth where the endometriosis could have been of transplantation origin.

An alluring feature of postsalpingectomy endometriosis is that the ectopic mucosa, which can be shown to have had its origin in the mucosa of a tubal stump and to have grown from it by continuous invasion, may not only retain the structure of the tubal mucosa, thus being actually an endosalpingosis, but may also assume both *the structure and function of the uterine mucosa,*

including its reaction to menstruation and pregnancy, thus producing true endometriosis. Even the endometriosis derived from the stump of the isthmus of the tube may be of uterine type. In the summaries of two previous papers published by the writer in the years 1928 and 1930, respectively, this feature of tubal stump endometriosis was stressed.

Mucosa of uterine type was present in the scars of all specimens of postsalpingectomy scar endometriosis which I have studied. In some specimens the endometriosis of the uterine cornu, which was proved to have been derived from the mucosa of the intramural part of the tube, was definitely of tubal type. However, after these tubules had penetrated the scar, typical uterine mucosa appeared in and about them. (See Case 4.) In other specimens the entire intramural part of the tube, which constituted the stump, was lined by mucosa of uterine type. The endometriosis of the cornu which had arisen from this mucosa, and the scar endometriosis continuous with it, were of uterine type. (See Case 2.) In my previous studies I had observed only a few instances in which the tubal mucosa of a stump had been replaced by mucosa of uterine type which was described by me as activated tubal mucosa. (See Figs. 10, 13, 16, and 32 of a previous paper.[4])

The most fascinating observation made in this study of postsalpingectomy scar endometriosis is the ease with which the gelatin, at times, flowed through the lumina of tubules and glands as though they were lymph vessels. In some specimens of scar endometriosis, tubules play the more prominent role and in others, glands; they are the leaders and life of the invasion. (Compare Cases 2 and 3.) A tubule is a Müllerian gland without appreciable stroma about it, and a gland is a Müllerian tubule clothed in stroma. Otherwise, Müllerian tubules and glands are essentially one and the same as far as the pathogenesis of postsalpingectomy endometriosis is concerned.

This work was done with the aid of the facilities afforded me in the Pathology Department of the Albany Medical College and the technical skill of Miss Helen Buchan.

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THERAPEUTIC ASPECTS OF UTEROTUBAL INSUFFLATION IN STERILITY*

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DURING the past three decades considerable progress has been made in the diagnosis and therapy of sterility. The very concept of sterility has been subjected to newer interpretations and qualifications. Thus Reynolds has suggested the term infertility to be applied to that group of women whose reproductive ability is temporarily lowered, the deficiency being amenable to treatment. Until recently, tubal obstruction was regarded as an absolute and irremediable cause of sterility. In 1919, Giles[1] considered "tubal disease one of the quite definite and incurable causes of secondary sterility as it is of primary sterility." This statement may now be qualified, due to progress made with use of uterotubal insufflation, to the use of x-rays combined with opaque media and other physical measures, exclusive of plastic surgery. By these nonsurgical measures, it has been possible to re-establish tubal patency in some cases when surgery is otherwise contraindicated or refused by the patient.

In the present paper, I have endeavored to estimate the therapeutic value of uterotubal insufflation in sterility. The study is based on the pregnancies that have taken place in my own series as well as the series reported by others. In my cases, no specific follow-up was made. The patients volunteered the information directly in some instances or they took occasion to transmit the report through the kindness of other patients whom they referred for diagnosis and treatment. For these reasons the percentages adduced lack definitive statistical value which only a complete and systematic follow-up would have yielded.

Although I have considered uterotubal insufflation primarily as a diagnostic procedure, its therapeutic possibilities have been stressed by others. First amongst these were Peterson and Cron[2, 3] and Rongy.[4] Since then there have been an increasing number of reports.

Modus Operandi.—The question of how insufflation aids the sterile woman, has from its inception engaged the interest of many. Peterson and Cron[2, 3] sought early in their experience with the therapeutic application of the insufflation test to explain the higher percentage of pregnancies in women who were secondarily sterile. They suggested that "something more than the mere passage of the gas and the mechanical opening of the tubes by insufflation must be considered." An exact explanation for the way in which insufflation aids the sterile woman cannot always be given. For the majority of successful cases, however, the therapeutic action appears to be the following:

1. *Establishing Patency of the Genital Tract.*—Insufflation establishes patency of the genital tract from the external os of the cervix to the abdominal

*Read by invitation before the Boston Obstetrical Society, March 20, 1945.

opening of the Fallopian tubes. Any cervical canal that is patulous to the uterine cannula employed in the procedure is ample for the entrance of spermatozoa. If the external os appears punctate or pin-point but admits the cannula, this is proof that it is wide enough to admit semen into the external opening of the cervical canal. The cannula at the same time stretches it somewhat, rendering the canal more patent for a varying period of time. Should intercourse take place shortly after this procedure, the spermatozoa have a better opportunity to enter the uterine cavity.

In this respect the procedure may be compared to the former practice of introducing a sound, which was frequently followed by pregnancy and believed by older gynecologists to be the result of the uterine sounding. In my series there was one case with a definite stricture of the cervix where the introduction of a uterine sound was shortly followed by pregnancy.

The patient was 27 years old and infertile for five years following the birth of a first child. She was examined just before an expected menstrual period which, however, was skipped, the Aschheim-Zondek test being positive two weeks later. Whether or not the sound had therapeutic value or was coincidental to an already existing pregnancy is not ascertainable. Strongly suggestive of the latter possibility is the fact that the procedure was carried out shortly before the next menstrual period. The case illustrates the difficulty commonly met with in endeavoring to give deserved credit to whatever measures may have been employed in sterility before conception takes place and the importance of analyzing all the circumstances connected with the case. The introduction of the cannula by itself has in all probability minor therapeutic value.*

2. *Removal of the Cervical Mucus Plug.*—In some cases a mucus plug, not visible at the external os but occupying the deeper portion of the cervical canal, is expelled after the cannula has been removed. I have the impression that the dislodgment of the mucus plug may be the important factor in a number of the earlier cases. In the past few years I have employed suction preliminary to the introduction of the cannula, thus clearing the cervical canal of the deeply lodged mucus plug.

Menchikoff[5] believes that the distention of the uterine cavity and the stretching of the internal os are often beneficial. Devraigne and Seguy[6] state that insufflation favors the ascent of spermatozoa by dilating the tubes in a way similar to dilation of the cervix.

3. *Effect on the Tubes.*—Insufflation probably exerts its most valuable therapeutic action on the tubes. Its manifold action consists in separating mild agglutinations of the folds of the tubal mucosa, straightening out tortuous tubes, especially of the infantile type (this must be only temporary), dislodging a mucus inspissation from a narrow to a wider portion of the tube, and actually separating adhesions at the fimbriated end in cases requiring pressures of 150 to 200 mm. Hg or more. In this manner a way is opened for the descending ovum to meet the ascending spermatozoa. Coghlan,[7] Hamant,[8] Floresco and Naum,[9] Geppert,[10] Rongy and Rosenfeld,[11] Sellheim,[12, 13] and others have offered this explanation, which was ventured in 1925.[14]

*In discussing this paper at Boston, Dr. John Rock stated that he had endeavored to check the value of introducing a uterine sound into the uterine cavity in 75 cases but encountered no pregnancy in his follow-up.

Hirst and Mazer[15] believe that the therapeutic action is often exerted on tubes which are nonpatent as a result of a blockade left in the wake of a catarrhal salpingitis which has remained unrecognized. With subsidence of this acute condition which is marked by increased secretion and thickening of the mucosa, accompanied by some destruction of the cilia, there still remains sufficient inspissated mucus in the tubal lumen to occlude it. They compare this condition to that found in the Eustachian tubes. "A retracted drum head means to an otologist insufficient ventilation of the middle ear due to occlusion of the Eustachian tube, structurally not unlike the Fallopian tube. To relieve this condition, the otologist resorts to inflation of the nasopharynx under pressure with the Pollitzer bag. He is frequently forced to make several attempts before he succeeds in opening the Eustachian tubes."

Peterson and Cron[2, 3] insufflated agglutinated tubes during laparotomy. When a pressure of 200 mm. Hg or more was reached, the gas was seen to be expelled into the peritoneal cavity either by a separation of the adhesions or by rupture of the infundibulum at the weakest avascular point of the tube, about 1 cm. from the closed fimbriated end. The opening, at first small, was enlarged by the continual escape of gas. They suggest the advisability of using high pressures, as high as 300 mm. Hg at operation, having found that in every instance rupture occurred at the infundibulum with no appreciable hemorrhage at any time. Either the adhesions separated or the tube ruptured at an avascular portion.

That pregnancy results from mechanical separation of adhesions through tubal insufflation has been observed at cesarean sections in the two following cases:

D. M., 29 years old, had been married for one year. She had a spontaneous miscarriage about three months after marriage and had not been able to conceive since then. On Aug. 7, 1933, tubal patency was demonstrated at a pressure of 208 mm. Hg, dropping in a parabolic curve to 68 mm. Hg. About three months later the patient conceived and was delivered by cesarean section on Aug. 29, 1934. Inspection of the adnexal regions showed that the right tube and ovary were bound down to the fimbria by adhesions which connected the tube and ovary with the posterior lateral aspect of the uterus. The adhesions connecting the left tube to the ovary were found to be broken and hung like long strands. These had evidently been broken through by the insufflation. Insufflation on Jan. 14, 1935, indicated tubal patency at a pressure of 99 mm. Hg. Auscultation was very loud on the left side and faint on the right side. About nine months later the patient conceived again, and was delivered by cesarean section, June 29, 1936. Insufflation on Feb. 16, 1937, showed retained tubal patency. (Figs. 1*A* and 1*B*.)

M. P. was a nullipara, married six years, with involuntary sterility for the past two and one-half years. Two and one-half years ago she had had an operation which was thought by the patient to have been a ventrosuspension and removal of her left tube and ovary. Uterotubal insufflation done elsewhere eight months ago showed tubal patency. The patient had always had severe dysmenorrhea, and hypomenorrhea had set in of late. During insufflation on Jan. 15, 1932, the pressure rose to 95 mm. Hg, then with further obturation rose to 172 mm. Hg, dropping to 128 mm. Hg. Fluoroscopy demonstrated a right subphrenic pneumoperitoneum. She conceived that same month, and was delivered by cesarean section, Oct. 7, 1932. At operation, the uterus was found fixed to the left by peritoneal and omental adhesions. The right ovary was found slightly enlarged, the right tube was bound down at the fimbria to the ovary and mesosalpinx by loose bands of adhesions. The left tube and ovary were absent.

Although artificial rupture can be free from harmful results, forcible opening of pathologic tubes requiring the use of high pressure should never be done deliberately except by the expert. With the abdomen open, higher pressures may be ventured. The possibility of producing gas embolism is obviated

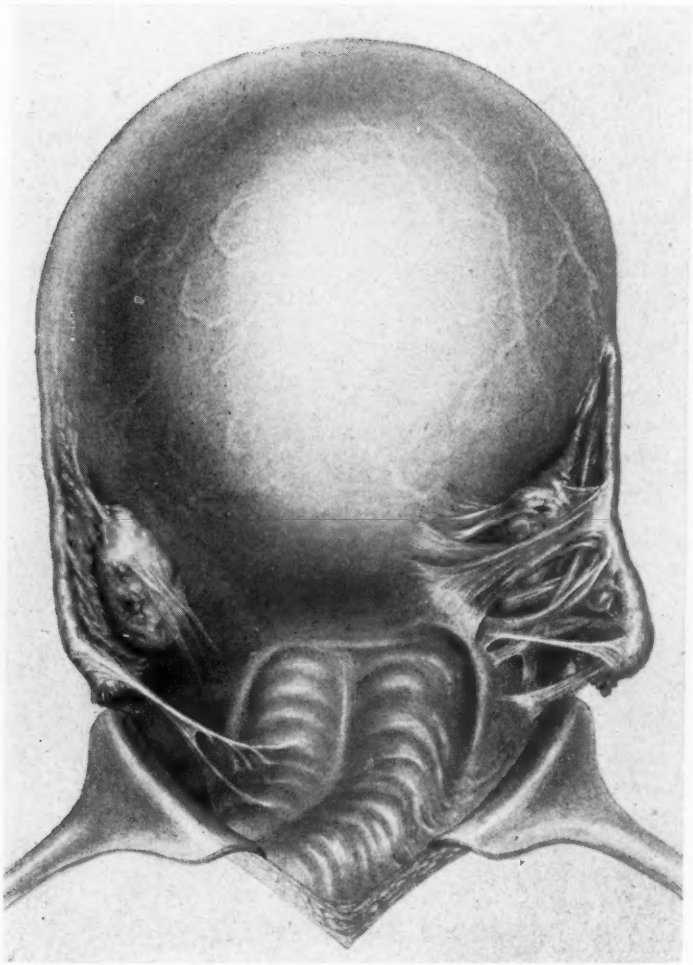

Fig. 14.—Both tubes are adherent to the ovaries. The fimbriated ends show through the adhesions, which are evidently fragmented, more especially on the left side. It is presumed that the ovum was carried through the left fimbria.

by careful avoidance of intrauterine trauma. This applies particularly when other gases, including air, are used instead of carbon dioxide, which has proved to be the gas of choice. Pressures above 200 mm. Hg have been employed by some individuals, using either gas or fluid. In the absence of palpable tenderness and of pelvic masses, careful uterotubal insufflation may be carried out, employing pressures beyond the recommended maximum with the prospect of opening tubes that resist lower pressures, the increment of risk to the patient being minimal.

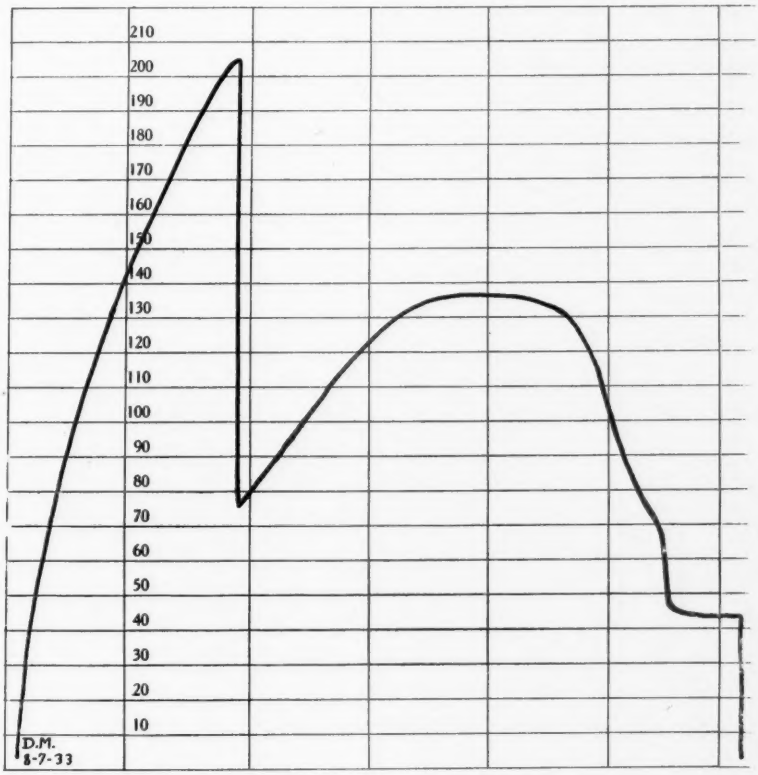

Fig. 1*B*.—Reconstructed tubograph, Aug. 7, 1933, showing an initial rise of pressure to 205 mm. Hg with a sharp drop to 76 mm. Hg, following which the pressure rose to 136 mm. Hg in a paraboloid fashion, dropping to 48 mm. Hg when the gas valve was shut. The fimbrial adhesions apparently of the left tube were broken through at 205 mm. Hg. as seen at the laparotomy for cesarean section.

Clinical experience with reopening ligated tubes by uterotubal insufflation illustrates the therapeutic value of this procedure with the convincing force of experimental corroboration. Figs. 2*A* and 2*B* show the tubographs in the first case in which ligated tubes were successfully reopened in this way.

The patient, D. S., aged 37 years, had had a cesarean delivery, at which time the Fallopian tubes were ligated. Contemplating remarriage after divorcing her husband, she wanted to know whether she could become pregnant again. This was made possible by uterotubal insufflation which opened the tubes at a pressure of 167 mm. Hg. She became pregnant shortly after her second marriage.

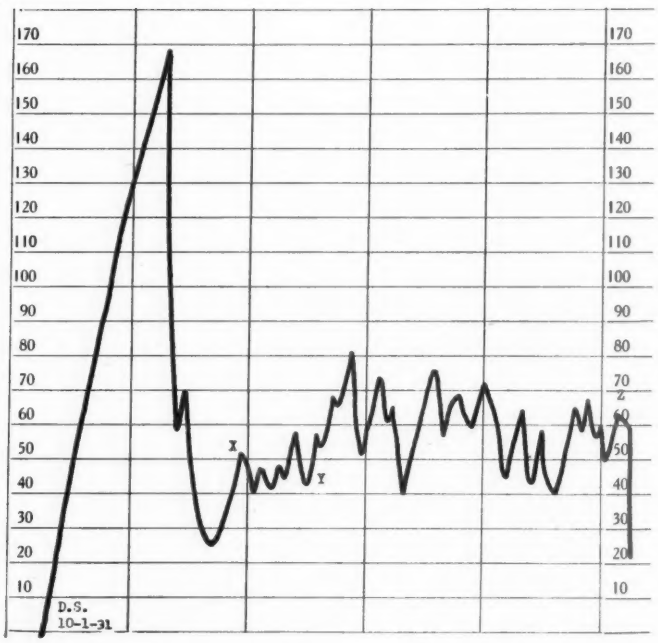

Fig. 2A.—Tubograph, Oct. 1, 1931, in case of patient D. S., showing the therapeutic effect of opening ligated tubes. Pressure rose to 160 mm. Hg, following which there was a sharp drop to 60 mm. Hg and to 25 mm. Hg, indicating the breaking through of the ligated tubes. Restoration of tubal patency and function is indicated in the graph from *x* to *z*. Pain was complained of on the left side at *x* and on the right side at *y*.

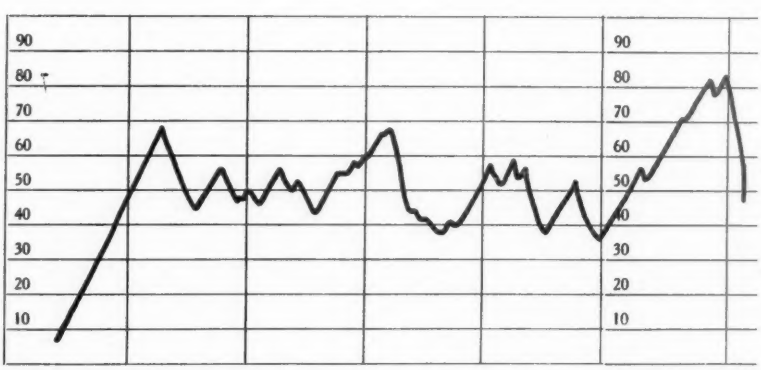

Fig. 2*B*.—Tubograph in the same case, Oct. 11, 1937, indicating normal tubal patency. Pregnancy had intervened between these two insufflations.

4. *Possible Psychic Effect.*—A factor not to be ignored is the psychic effect produced by uterotubal insufflation. Although the exact mechanism is not clear, there are women who respond to insufflation through the psyche acting on the autonomic nervous system. Whether or not this results in a relaxation of otherwise spastic tubes must await further inquiry.

We have met, in certain tubes, with spasms sufficient to close the uterine ostia in a manner similar to the closure of the internal os of the cervix. Overcoming such spasm may obviously exert a therapeutic effect. Pouliot[16] reports two instances of uterotubal spasm where pregnancy followed insufflation. I have had a similar experience in twenty cases.

Another possibility is the occasional hastening of follicle rupture, particularly in women whose emotional psychic reaction to the insufflation inaugurates an orgasm during the next marital relation when it would otherwise be absent. The matter of coincidence must be considered in this respect. No actual proof is at hand of an ovulation thus provoked. Whether the psychic reaction produces on some occasions follicle rupture similar to that which invariably follows coitus in the rabbit is purely a matter of speculation and falls into that category of suggestive therapeutics of which the Fliess treatment affords a notable example.

Lane-Roberts, Sharman, Walker, and Wiener,[17] bearing in mind the possible stimulating effect of insufflation upon the endocrine system, prefer to withhold its use to the month preceding the cycle during which investigation of the hormonal functions in any given case is carried out. These authors state that "although there is no definite evidence that the therapeutic results of this procedure may be accounted for in part by its stimulating effect on endocrine function, this possibility cannot be wholly excluded."

5. *The Therapeutic Effect of Repeated Tests.*—When the tubes were found to be obstructed, the test was repeated not only for diagnostic corroboration but also for its therapeutic effect. For this purpose as many as 18 tests were performed on one of my personal cases.

A therapeutic tubal effect may be deduced under the following circumstances: (1) when the initial rise of pressure is lower at a second or third insufflation, and (2) when the level at which the pressure is maintained is likewise lower. Not infrequently one meets with a return of tubal function which is demonstrable on the kymograph.

A most striking therapeutic result was seen in women whose tubes were insufflated several times, nonpatency being encountered at a first or second test and patency at a subsequent test, and who became gravid shortly after the last insufflation. Under these circumstances it seemed justified to credit insufflation with the successful result. Twenty patients in my series, in whom a single test showed a pressure of 200 mm. Hg, nevertheless became gravid. In these cases either a small amount of gas was forced through strictured tubes, the amount being insufficient to produce a subphrenic pneumoperitoneum and shoulder pains, or uterotubal spasm actually resisted the passage of CO_2 at a pressure of 200 mm. Hg.

Repeated ectopic pregnancy may result despite pressure of 200 mm. Hg or more being encountered during insufflation.

This was found in the case of R. A., a 33-year-old woman, who had a right salpingectomy for ruptured tubal pregnancy, two years after marriage. Repeated uterotubal insufflations with pressures of 200 mm. Hg or more produced no shoulder pains and no subphrenic pneumoperitoneum, thus indicating an obstructed residual tube. One year after the last insufflation, she was operated on for ruptured ectopic gestation in the left tube.

To what extent repeated insufflation may improve the tubal status from high-grade strictures to varying degrees of patency may be seen in Table I.

TABLE I. THERAPEUTIC EFFECT OF REPEATED TESTS

	NUMBER OF TUBAL CASES	NUMBER OF IMPROVED	PERCENTAGE
Tubal obstruction; maximum pressure 200 mm. Hg	939	185	19.70
Adherent and strictured tubes; maximum pressure 200 mm. Hg or less	917	238	25.95
Uterotubal spasm; maximum pressure up to 190 mm. Hg	134	15	11.19

Altogether, there were 438 patients whose Fallopian tubes showed improvement in patency on a second or third insufflation. Sixty-six of these women became pregnant (15.07 per cent). It is noteworthy that 79 of the 238 patients with adherent and strictured tubes showed a normal curve following several insufflations.

In Weitzner's[18] series of 250 sterility cases, tubal obstruction was reduced from 38 to 27 per cent by a second insufflation. Abbott[19] reported a series of 51 cases of occluded tubes. Four of these patients became pregnant following the opening of the tubes by repeated insufflations; no other measures had been employed. Twenty-eight other patients became pregnant following repeated insufflations combined with other forms of therapy.

In Douay's[20] series of 100 women with "closed" tubes, patency resulted after repeated insufflations in 18 cases; 5 of these became pregnant (28 per cent). Graff[21, 22] found 44 per cent of his patients to have nonpatent or partially obstructed tubes. Twelve per cent of his cases became patent after repeated tests, and of these 14 of 43 cases became pregnant (32.6 per cent). Davis[23] succeeded in opening the tubes under pressure in 8 of 13 cases with "closed tubes" and 3 of these patients became gravid.

Pouliot[16] observed 14.4 per cent pregnancies, i.e., 24 of 167 women with permeable tubes, whereas 14 of 43 women whose tubes were made permeable became gravid, i.e., 32.6 per cent. In Meaker's experience, the gas passed through the tubes after much difficulty in the first trial in two patients and in another patient only at the fourth attempt. Two of these patients became gravid at once and the other after two months.

Mintz[24] established patency in 25 out of 44 cases by repeated insufflation and diathermy. Eleven of these patients became pregnant.

The results just mentioned in a combined series aggregating over one thousand cases call attention to the fact that we must revise our notion of what constitutes tubal closure and it becomes necessary to define the term "closed tubes." A hydrosalpinx is the classic representation of a closed tube which is watertight and therefore airtight. The clubbed fimbriated end is another example of a closed tube. There are, however, many degrees of nonpatency, varying from the mild agglutination of a few mucosal folds to light adhesions about the fimbria, including phimosis, all of which may be said to render the tubes unfit for their physiologic function, namely, to convey the ovum toward the spermatozoa.

There is no doubt that occasionally these impediments disappear spontaneously, permitting conception to take place, and pregnancy develops normally. Not infrequently, however, the impregnated ovum is trapped in the tube or more rarely even in the ovary.

As we have seen, thanks to Peterson's experimental observations during laparotomy, closed tubes in the truest sense may be opened by employing sufficiently high pressures. In many of the other relatively closed or nonpatent tubes it is possible to widen the strictured lumen by more moderate pressures. From the therapeutic point of view this is of the greatest importance, as experience has repeatedly demonstrated.

We are, therefore, in a position to state that, within certain clinical and pathologic limits, practically all Fallopian tubes fall into three groups: (1) normally patent tubes; (2) nonpatent tubes; (3) intermediary. With adequate pressures, Group 2 may be advanced to Groups 3 and 1; Group 3 may be more readily restored to Group 1, i.e., normality.

Group 1 refers to tubes where patency is demonstrable upon the first trial with insufflation, the pressure noted being at 100 mm. Hg or less, and good contraction waves or oscillations are recorded on the kymograph. Group 2 includes tubes that do not yield to pressures of 200 mm. Hg in two or three tests. Group 3 includes tubes that show relatively high pressures but some slight patency in the first or second test.

The extent to which some degree of patency can be produced by tubal insufflation alone or by any additional measures, such as diathermy treatment or the more potent hormonal extracts, will determine the conceptional possibilities in women whose sterility is traceable chiefly to tubal pathology. It is with this object in mind that the following statistical analysis has been made in 590 personal cases of pregnancy preceded by uterotubal insufflation.

Five hundred and ninety cases of pregnancy occurred after insufflation in 3,200 cases. The well-known tendency of ascribing to any new method of treatment an occasional successful result in the sense of *post hoc ergo procter hoc* applies equally to insufflation. There is no doubt that many patients have become pregnant after a shorter or longer interval following an insufflation which has demonstrated normal tubal patency. Obviously the diagnostic test may have had no etiological connection, the ever-present element of chance and coincidence playing its part. In order to offset this it has seemed to me necessary to venture certain reasonable criteria which would serve more adequately to estimate the therapeutic value of insufflation.

A therapeutic result may be deduced when the following conditions are met:

1. The age of the woman is 30 years or over.
2. The length of marriage is three years or longer.
3. No other therapeutic measure was employed.
4. The insufflation was done within the first two weeks of a last regular period (in preovulation phase).
5. No contraceptive precautions were taken for at least one year prior to the test.
6. Pregnancy follows within a month or at most two months after tubal insufflation.

7. Pregnancy follows after repeated insufflation; a relatively lower pressure sufficing to demonstrate patency on a second, third, or fourth test.

8. Pregnancy follows the third month after one insufflation during which a high initial pressure was necessary and the tubes were found to be strictured or adherent. Obviously the element of chance may be regarded as minimal.

Primary Versus Secondary Sterility.—In my personal series there were 2,014 patients in the group of primary sterility. Of these, 358 (17.77 per cent) became gravid. There were 1,186 patients with secondary sterility of whom 232 (19.56 per cent) became pregnant. Altogether, 590 women were reported pregnant out of 3,200 cases, making the total percentage 18.44. This percentage may not be taken as final because only 590 patients voluntarily reported their pregnancy either directly or through a patient referred by them for treatment.* It is probable that others may not have thought it of interest to communicate the fact of their pregnancy at once or later, while a not inconsiderable number remember to do so after the birth of a second or possibly third child. For obvious reasons a routine follow-up questionnaire was not submitted to patients. In a number of instances the report came from the family physician. Inquiry of colleagues employing tubal insufflation had been made in 1928, the response to which has been tabulated. An additional series was reported by a larger number who replied to a recent questionnaire.

To what extent insufflation was helpful in the 232 cases of secondary sterility may be seen from the way in which the pregnancies had terminated prior to treatment (Table II).

TABLE II. PREVIOUS PREGNANCIES OF 232 SECONDARY STERILITY CASES

	NUMBER	PERCENTAGE
Term babies	74	31.8
Tubal pregnancies	19	8.2
Stillbirths	11	4.7
Spontaneous abortions	70	30.2
Induced abortions	35	15.1
Abortions—type not stated	23	10.0
Total	232	100.0

The slightly greater success following insufflation in the secondary sterility cases may be mere coincidence (19.56 per cent as compared with 17.77 of primary sterilities). On the other hand, since these patients had already demonstrated their ability to conceive, it may indicate the more frequent occurrence of tubal obstructions as a result of puerperal or abortal infection, which the mechanical act of insufflation may be credited with overcoming.

Age of Patients.—The age of patients who became gravid is important from the standpoint of the therapeutic effect, as it must be in considering the value of any other therapeutic measure that might be employed in sterility (Table III).

One hundred and forty-six patients were between the ages of 20 and 25 years, and 250 between the ages of 25 and 30 years. One hundred and eighty-

*Since the collection of the above data 82 additional cases have been recorded. The statistics were compiled by Dr. Morris Feresten.

TABLE III. AGE OF PATIENTS

AGE (YEARS)	NUMBER	PERCENTAGE
15-20	10	1.69
20-25	146	24.75
25-30	250	42.37
30-35	144	24.41
35-40	34	5.76
40-45	6	1.02
Total	590	100.00

four, or 31.19 per cent, were 30 years of age or over when they sought relief; 34 of these were between the ages of 35 and 40 years, and six were over 40 years old.

Length of Marriage.—In any consideration of the treatment of sterility, it is important to take into account the question as to how long after marriage we shall wait before encouraging a married couple to seek relief from sterility. A period of three to four years has been previously regarded as ample time to judge whether a marriage is sterile. This figure is obviously arbitrary, for some women have become pregnant long after this interval. On the other hand, serious difficulties in the way of conception may exist soon after marriage and not infrequently even before marriage. Giving Nature a prolonged trial in such cases merely delays corrective treatment which may require a relatively long period of time. Other things being equal, the younger the patient is, at the time the cause of her sterility is discovered and removed, the greater are her chances to benefit by treatment.

TABLE IV. DURATION OF MARRIAGE

DURATION (YEARS)	NUMBER	PERCENTAGE
1- 3	225	38.14
3- 5	154	26.10
5-10	170	28.81
10-15	38	6.44
15-20	3	0.51
Total	590	100.00

In this series, 225 women, or 38.14 per cent, were married from one to three years when they sought relief from childlessness (Table IV). The reasons why these patients applied for relief early were varied. Thus, one young woman was ardently desirous of an offspring for reasons concerning the settlement of an estate. Another had witnessed the difficulty encountered by two older sisters who became pregnant from three to five years after marriage. One patient was over 40 years of age and felt that she had only a short childbearing period left to her. She sought advice within a few months after marriage. Several had been married to a first husband for a number of years without conceiving. Consummating a second marriage, it was not surprising that they endeavored, after waiting only a short time, to discover the cause of their infertility. A few had had an only child and dreaded the thought of bringing up a solitary child.

Thus, there are various circumstances, social, economic, domestic and some of private personal nature, that impelled this small group of patients to seek a

solution. The majority (61.86 per cent), however, had been married over three years, 41 having been married ten years or longer.

Average Time of Conception Expectancy.—In any analysis of the end results of a therapeutic procedure in sterility it is well to take into account the natural expectancy of conception among couples after variable lengths of married life.

Coghlan[7] found that only 295 women, approximately 3 in ten thousand, out of 1,001,383 married women in Australia had a first child after being married ten years or longer. He estimated the incidence of a first pregnancy in women married fifteen years or over at 0.005 per cent (one in twenty thousand).

G. Kaboth and J. Kleefisch[32] analyzed the marital history of 5,331 couples in order to estimate the natural incidence of spontaneous conception. Their figures serve the useful purpose of comparison with the results obtained by therapeutic measures applied in the treatment of sterility.

In my series of cases of secondary sterility, the length of time elapsing from the last pregnancy, whether it terminated in abortion or full-term pregnancy, was reckoned as equivalent to a period corresponding to the duration of primary sterility. If contraceptive measures were used, the period of involuntary sterility was measured by the interval elapsing from the time they were discontinued. (Table V.)

TABLE V. DURATION OF STERILITY (PRIMARY AND SECONDARY)

DURATION (YEARS)	NUMBER	PERCENTAGE
1- 3	285	48.31
3- 5	162	27.46
5-10	127	21.53
10-15	14	2.37
15-20	2	0.33
Total	590	100.00

Comparison With the Natural Expectancy of Conception.—After the third year, three times as many patients became pregnant as might be expected according to natural incidence. After seven years, the patients' chances are increased many times by insufflation; and after ten years, according to Coghlan's estimates, insufflation appears to improve proportionately the chances of pregnancy. The two patients who became pregnant after having been sterile for fifteen years show an incidence of one in 1,600, as against one in 20,000 according to Coghlan's figures. When it is considered that 34 of my patients were between the ages of 35 and 40 years, and six were over forty years, the 40 pregnancies in this group may be accepted as due to therapeutic efforts rather than chance.

Use of Contraceptive Precautions.—Of the 590 patients who became gravid following insufflation, 190, or 32.20 per cent, had used precautions at some time of their marital life. In 97 of these, an interval of at least two years had elapsed since they stopped contraceptive precautions. Fifty-four patients had used no precautions for three to seven years before seeking relief. The remaining 39 patients had ceased the use of precautions for one year before insufflation.

Many women employ precautions only to find out to their surprise, after discontinuing the practice, that they cannot become pregnant. How the use of

preventive measures affects the reproductive organs of the female, rendering her less susceptible to conception is still a matter of conjecture. It may be presumed that the use of chemicals such as Lysol douches, bichloride of mercury and even less corrosive solutions possibly alter the vaginal and cervical mucosa and their normal secretions. The bacterial flora which are usually present in the vagina, and which favor the spermatozoa, may possibly be disorganized by the frequently repeated use of antiseptic douches, pessaries, and other devices. On the other hand, the practice of withdrawal is not unlikely attended by sequelae as yet not understood, which may exert a deleterious influence on the mechanism of conception. It must, however, be noted that a not inconsiderable number of women practice contraception whose Fallopian tubes are blocked and hence could not conceive if they took no precautions, while, in some cases at least, the male may be sterile without knowing it.

The Male Factors.—In analyzing the factors involved in sterility we cannot omit the male factor. It is important to note the degree of potency and character of the sperm output. Many women, already handicapped by their own lowered fertility, were still further burdened by a mate with reduced fertility. In some cases, the male alone may have been responsible for the sterility. None of the patients in this group were insufflated until there was satisfactory evidence of intromission and the production and quality of the sperm were determined. The Huhner test was employed and whenever necessary the unmixed specimen of semen was examined. If the wife came from some distant town unaccompanied by her husband, the data concerning the male partner were usually furnished by the family physician. Such information was obtained in 66 cases.

In 320 cases the husband was considered potent and satisfactory. In 193 cases there was a mild oligospermia; 64 of these, as demonstrated by later examinations, showed improvement after treatment by diet, advice about coitus, and the like.

Eleven husbands had a marked oligospermia. In 10 of these cases the spermatozoa were so few that they could not be found in the vaginal or cervical secretions when a single Huhner test was made; in another case two examinations failed to reveal the presence of spermatozoa. In these 11 cases, a condom examination, were it feasible, might have shown the presence of spermatozoa. Unless the patient frankly avows the resort to substitution, it is naturally impossible by the Huhner test alone to determine the fertility of the legitimate mate. This criticism applies equally to the examination of the condom specimen.

In a number of cases there was lowered fertility of both the male and female partner. Improvement in tubal patency following insufflation of tubes which were partially occluded, and improvement in the seminal output on the part of the husband raised the combined fertility to a point where conception took place. Occasionally, inseminating the wife artificially at such a favorable time results in pregnancy after one trial.

This was encountered in L. T., a 24-year-old woman who had been married for four years without being able to conceive. Uterotubal insufflation done elsewhere showed incom-

plete tubal obstruction, shoulder pains appearing after one-half hour. On Nov. 30, 1926, a kymographic insufflation showed obstruction to a pressure of 150 mm. Hg, when there was a gradual drop to 100 mm. Hg, after which shallow oscillations were recorded. The husband had oligospermia, for which he was later treated. On March 21, 1933, the tubes were found to be obstructed at a pressure of 190 mm. Hg when the gas passed through, the pressure dropping to 115 mm. Hg, following which shallow oscillations were again recorded. On Jan. 30, 1934, the obstruction was noted at a level of 205 mm. Hg at the first insufflation. The gas began to flow through at the second trial at 200 mm. Hg. At this time there was present uterotubal spasm in addition to stenosis which was characterized by pain and discomfort localized at the midline above the symphysis pubis. The patient was extremely desirous of becoming pregnant and, having brought in a sterile jar an ejaculate of semen which proved to be normal in all respects, the semen was poured into the vagina where it was left for an hour while the patient lay in the Trendelenburg posture. She conceived promptly and had a normal child Oct. 10, 1934.

Subsequently, Feb. 19, 1937, uterotubal insufflation showed normal patency and good oscillations indicating good rhythmic tubal contractions (Fig. 3).

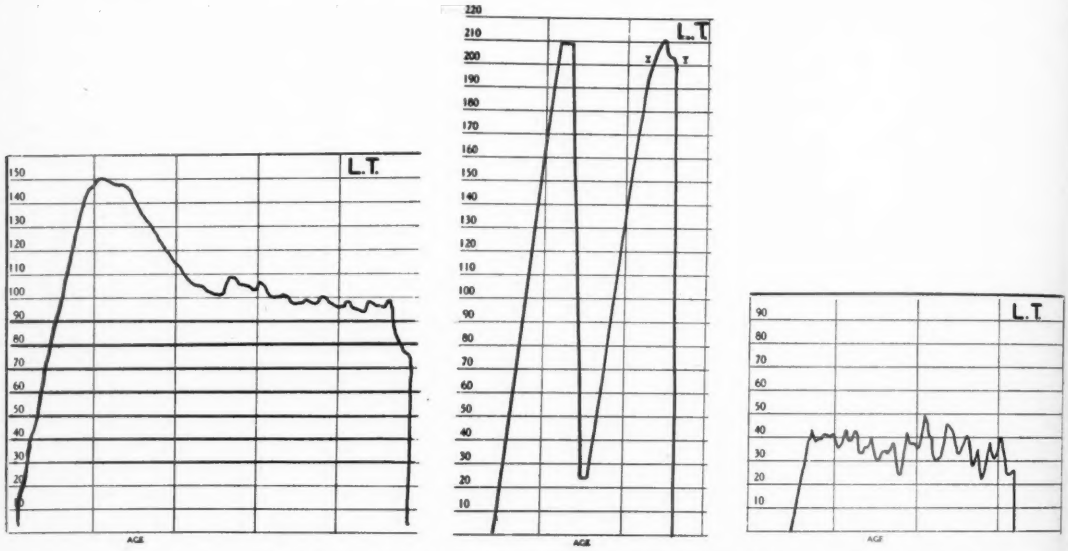

Fig. 3.—*A*, Tubograph, Nov. 30, 1926, showing tubal narrowing. *B*, Tubograph, Jan. 30, 1934. Note *xy*, the rounding of the curve, indicating a slight degree of patency in addition to spasm. *C*, Tubograph, Feb. 19, 1937, showing practically normal tubal patency and function as a result of intervening pregnancy with its estrogenic influence on the tubes.

The Tubal Factor.—Insufflation was the only treatment employed in 386 of the 590 patients who became pregnant (65.42 per cent). The therapeutic measures employed in the remaining 204 cases are too varied for evaluation.*

Table VI shows that 46.44 per cent of the pregnancies occurred in women whose Fallopian tubes exhibited various degrees of impaired patency.

The incidence of pregnancy in the general sterility group according to the status of the tubes is shown in Table VII.

*Important as they are in considering general therapeutic treatment in sterility which includes artificial insemination, details concerning them are not entered into here because it is our special task to evaluate the tubal factor. In this connection it may be well to emphasize the desirability of determining the fact of tubal patency before subjecting the patient to an artificial insemination.

TABLE VI. TUBAL STATUS IN 590 PATIENTS WHO BECAME PREGNANT

	NUMBER	PERCENTAGE
Normal patency	316	53.56
Adherent tubes	135	22.88
Strictured tubes	118	20.00
Spasm and normal patency	21	3.56
Total	590	100.00

TABLE VII

	NUMBER OF CASES	NUMBER OF PREGNANT CASES	PERCENTAGE
Normal patency	1,210	316	26.12
Adherent tubes	538	135	25.09
Strictured tubes	379	118	31.13
Spasm and normal patency	134	21	15.74
Total	2,261	590	98.08

The therapeutic effect of insufflation is particularly noteworthy in the 118 cases of strictured tubes which resulted in pregnancy in 31 per cent as against 26 per cent of the cases with normal tubal patency.

There were five additional cases with incomplete tests who became pregnant. The cervical canal was strictured in one case; the uterine cavity was probably not entered but the patient promptly became gravid.

In one case a pressure of 200 mm. Hg was reached. The patient weighed 160 pounds, and, as about 60 c.c. of gas was introduced, only the smallest part of it entered the peritoneal cavity through the strictured or spastic tubes. There was insufficient gas to produce a visible pneumoperitoneum or shoulder pains, and the patient was advised to have the test repeated the following month. This was not necessary as she became pregnant the same month. In another case the gas passed through freely at a low pressure but not enough gas was introduced to produce the typical subphrenic pneumoperitoneum and shoulder pains. She became pregnant. In one case the first and only insufflation showed a pressure rise to 160 mm. Hg and all the indications of patency were not present. In the fifth case data were lacking for a diagnosis of the tubal status.

Occasionally the fluoroscope fails to reveal a subphrenic pneumoperitoneum although the pressure shows a definite tendency to drop from a high level during the insufflation, indicating some degree of tubal patency which is further substantiated by the appearance of shoulder pains. In such cases I have felt that the diagnosis of patency should be held in abeyance till all the signs and symptoms of a subphrenic pneumoperitoneum are manifest. Should it be important to make the diagnosis at once, it is only necessary to prolong the flow of gas for another minute or two, when all the pathognomonic signs and symptoms may be elicited. This small group with incomplete tests has an interesting relationship to the therapeutic aspects of insufflation. As only 5 of the 142 women (3.5 per cent) who were classified amongst the incomplete tests became pregnant, compared to an average of 18.43 per cent who had a complete test, it may be construed as a check on the therapeutic efficacy of insufflation.

Initial Rise of Pressure.—The initial rise of pressure at which the gas passed the uterotubal junction in these 590 cases gives us another angle from which to judge the therapeutic effect of uterotubal insufflation.

TABLE VIII. INITIAL RISE OF PRESSURE

	NORMAL PATENCY	ADHESION	STRICTURE	SPASM
Under 50 mm. Hg	28			
50 to 100 mm. Hg.	241	74		
100 to 150 mm. Hg	47	61	35	10
150 to 200 mm. Hg			54	8
200 mm. Hg plus			29	3

Of the 590 patients, 247 or 41.86 per cent, had initial pressures above 100 mm. Hg, which may be taken as evidence of impaired patency. The therapeutic effect of insufflation is particularly noteworthy in the 94 cases in which pressures of 150 mm. Hg and over were required for the gas to pass through the tubes.* Repeated insufflations improved the status in many of these cases before pregnancy took place. Thus, among the patients who became pregnant following insufflation, the test was repeated once in 104 patients, twice in 37 patients, three times in 16 patients, four times in 10 patients, five times in 3 patients, six times in 5 patients, seven times in each of the 4 remaining patients. These 179 patients had therefore received 526 tests before they became pregnant, or an average of approximately 3 to each.

Use of the Kymograph.—The value of the kymograph in these cases cannot be overestimated. It has been used by me in conjunction with tubal insufflation since May, 1925, and particularly in connection with prognosis and therapy it affords appreciable aid. Of the 590 patients who became gravid, 544 were examined with the kymograph. Thanks to increased experience gained through the use of this instrument, it has been possible to repeat the test both with greater intelligence and with more gratifying results. Forty-nine patients had been insufflated elsewhere.

Tubal Insufflation Followed by Lipiodol Injection.—In 7 of the successful cases with high-grade strictures, lipiodol was also employed. In 3 cases insufflation had been done once before lipiodol was employed; in 3 cases three times and in one case four times. In 4 of these cases insufflation also followed the lipiodol injection, once in 2 cases, four times in one case, and seven times in the other before pregnancy ensued.

The therapeutic efficacy of lipiodol in these 7 cases is difficult to appraise because altogether 29 insufflations had been done before or after the 7 single lipiodol injections. I have had occasion to inject lipiodol in 159 patients and pregnancy followed insufflation and lipiodol in these 7 patients alone. If we omit 99 cases of tubal closure and the 7 cases in which the examination was unsatisfactory, the incidence of pregnancy in the remaining 53 cases is 13.21 per cent. This is less than half the percentage of success where insufflation alone was employed in the general group of patients having tubal strictures (31.13 per cent).

*Rucker[25] found that when the tubes were open, pregnancy followed in more than 23 per cent; when partially obstructed, it followed in 20 per cent; and when tighter strictures were present, pregnancy occurred in 33 per cent of his cases. Moench[26] observed one pregnancy out of 33 patients with obstructed tubes and 7 pregnancies in 55 cases with open tubes. Baer[27] reports 2 cases and Seymour 1 case with high-grade tubal strictures that became gravid after insufflation. In Morgan's[28] 8 successful cases, 5 had partial tubal obstructions. In Fuchs' 9 cases, high pressure was required in 6; 3 of these cases became gravid within two weeks, 1 within six weeks, 1 within four weeks, and the sixth became pregnant four months after insufflation. Monbach[29] reports 4 pregnancies out of 11 cases with high-grade strictures, and 3 successes out of 14 cases with milder strictures. Francillon-Lobre and Dalsace[30] observed 5 pregnancies in 27 cases; 3 of these cases had high-grade strictures.

Radium and X-ray Therapy.—Of the 590 cases of pregnancy, 11 were treated with small doses of radium for delayed and scanty periods and one received a larger dose for menometrorrhagia. Eight of the 12 patients became gravid within one year of the use of radium, 4 within the first six months. Similarly, 29 patients had received x-ray and insufflation therapy before becoming gravid. As all of these patients were insufflated before receiving x-ray or radium therapy, it is difficult to say how much credit for the successful outcome should be alloted to these measures, especially as insufflation of the tubes often intervened between the "stimulating" treatments and pregnancy.

Time of Pregnancy in Relation to Insufflation.—The time elapsing between insufflation and conception was noted. Data were available in 573 cases.

TABLE IX. TIME OF PREGNANCY IN RELATION TO INSUFFLATION

NO. OF PREGNANCIES	TIME AFTER INSUFFLATION
158	Within 1 month
70	Within 2 months
37	Within 3 months
38	Within 4 months
35	Within 5 months
40	Within 6 months
49	Within 2 years
15	Within 3 years
9	Within 4 years
5	Within 5 years
3	Within 6 years
3	Within 7 years
2	Within 8 years
1	Within 10 years

Three hundred and seventy-eight, or 64.07 per cent, of the pregnancies occurred within six months of the test; 108 pregnancies occurred within the second six months.

In 17 cases the time interval was not recorded.

It is noteworthy that 228 patients or 38.64 per cent became gravid within two months after insufflation. This short interval appears to be a fair criterion of the therapeutic value of the method. Many of these patients had been married or sterile five years and longer, a fact which is supportive proof of its efficacy. Obviously, the test cannot be held to have produced a remedial result when more than two regular menstrual periods have intervened between its use and conception except in cases where strictures were encountered. In cases where insufflation has demonstrated normal tubal patency, one can speak only of its diagnostic and prognostic value. The fact that 38 women became gravid in my series after an interval of two years or more following insufflation should cause us to hesitate to give a hopeless prognosis for childbearing when the Fallopian tubes have been found patent or where they have been rendered patent.

The case of L. W. is an example. This 23-year-old woman, sterile for two years, was first seen in 1925. Physical examination was essentially negative except for palpable left adnexa. Repeated uterotubal insufflations indicated nonpatent tubes. The findings at laparotomy in 1929 were: retroverted adherent uterus with several fibroids; right hydrosalpinx with periovarian adhesions; left tube adherent in the pelvis, the fimbriated end how-

ever appearing free. The peritubal and periovarian adhesions were separated, the fibroids were enucleated, the right tube was excised, and the uterus was ventrosuspended. The left tube, before being freed of adhesions, was insufflated through the uninvolved fimbria and showed an obstruction. Retrograde fimbrial insufflation after the left tube was straightened out proved it to be patent down to the uterine end. Three years later, in 1932, she became pregnant and was delivered by cesarean section. In 1941 another pregnancy went to term, and delivery was by cesarean section. At this time the patient at her request was sterilized by tubal excision. Histologic examination of the left tube showed no noteworthy changes. The right tubal stump showed chronic salpingitis with decidual reaction of the mucosa.

The Eventuality of Pregnancy.—The data as to the outcome of pregnancy are available in 517 women who became gravid after insufflation in my series. Of these, 419, or 81.04 per cent, had 490 full-term babies; 191 of these were boys, 183 girls, and in 116 the data are lacking. Patients under my own care during pregnancy numbered 254. Of the 250 patients who were personally delivered, 208 or 81.80 per cent had full-term children.

TABLE X. THE EVENTUALITY OF PREGNANCY IN 517 CASES

	NUMBER OF CASES	PERCENTAGE
Term babies only—born alive	383	74.08
Premature babies—born alive	4	.77
Premature and term babies—born alive	4	.77
Premature and incomplete abortions	2	.39
Stillbirth at term	2	.39
Stillbirth	2	.39
Spontaneous abortions	81	15.67
Spontaneous abortions and term babies	26	5.03
Tubal pregnancy—born alive	9	1.74
Tubal and term pregnancies—born alive	4	.77
Total	517	100.00

Many of the patients who aborted belonged to the amenorrhea group. They were not aware of their pregnancy until bleeding began. From my study of these particular women with habitually delayed periods, they appear to exhibit a greater tendency to abort than women with normal menstrual function. On the other hand, the salvage of babies in the cases treated for secondary sterility is particularly striking. Undoubtedly greater care during the pregnancy following therapeutic treatment accounts for the increased number of full-term babies (84 per cent compared to 32 per cent, Table II).

Ninety-four patients who became pregnant following insufflation subsequently encountered renewed difficulty in conceiving. Another insufflation was again succeeded by pregnancy. In 22 of these cases, high-grade strictures were demonstrated by the insufflation preceding the second gravidity.

After an intervening pregnancy the kymographic curve may change, showing some degree of obstruction or improved patency. On the other hand, it may show the same or similar characteristics. Two examples may be cited in this connection:

M. R. was a 26-year-old woman, sterile for almost three years. Physical examination was essentially negative except for the hypoplastic uterus. Repeated uterotubal insufflations indicated uterotubal spasm. During one insufflation performed about two weeks after a

menstrual period, the curve was essentially normal and the tubes were definitely patent. Coitus was advised for that and the next day, and gestation ensued the following month (Fig. 4).

E. E., a patient with secondary sterility, showed evidence of strictured but partially patent tubes at insufflation, Dec. 9, 1929, when the pressure rose to 200 mm. Hg in a somewhat paraboloid curve with a tendency to drop slowly. On repeated insufflation on the same date, pressure rose to 192 mm. Hg with a sharp drop to 38 mm. Hg, without any audible external regurgitation from the cervix. She had a subphrenic pneumoperitoneum and shoulder pains. The patient became pregnant the same month and had a missed abortion six months later. A second insufflation, done Dec. 12, 1930, showed tubal patency at low pressure levels with atypical fluctuations.

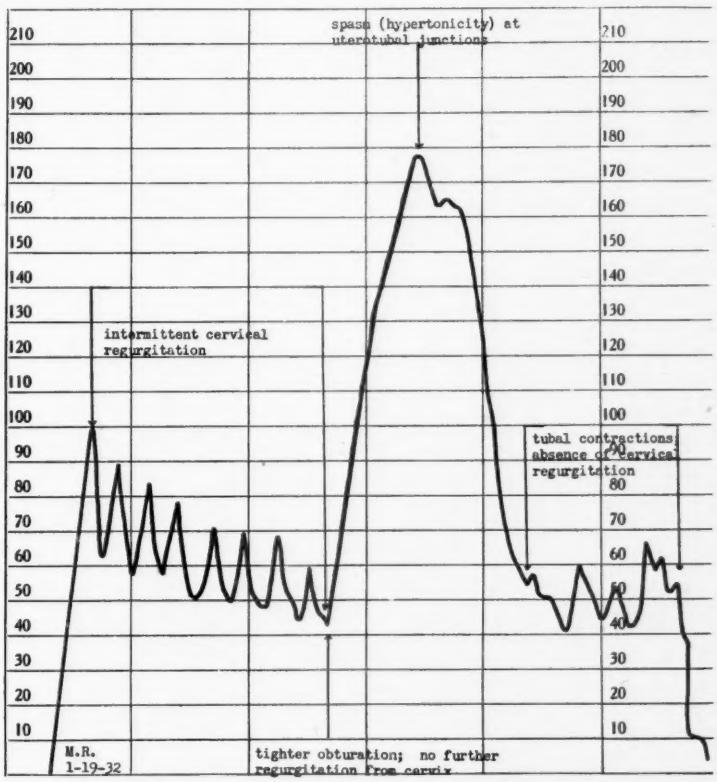

Fig. 4.—Tubograph, Jan. 19, 1932, in case of uterotubal spasm.

The discrepancy in the percentage of successful results obtained by various observers is probably due in general to differences in the cases selected for insufflation, to the possible variations in technique, and to the follow-up of their patients.

To the results already mentioned may be added those of Pribram,[31] Kaboth,[32] Samuel,[33] and Sellheim[34] who have concluded that, though the statistical incidence of pregnancy following insufflation cannot be estimated with precision, the method has a value which makes it indispensable in the treatment of sterility. It is not unreasonable to suppose that if the exact outcome of all patients insufflated were known, the sum total of pregnancies would be greater than the reports indicate.

Proof of Therapeutic Efficacy.—If one judges results according to the rigid demands of the criteria for a therapeutic result, we have 26 cases which have fulfilled all the requirements. These 26 cases were women who became pregnant within one month following this procedure. They were over 30 years of age, were sterile for a period of over five years, took no contraceptive precautions for at least one year, and resorted to no other treatment than insufflation. Excluding most of the other cases, there remain 66 in whom a therapeutic action on the part of insufflation is suggested because pregnancy followed upon improvement in the tubal status as a result of repeated insufflations.

In estimating therapeutic results or etiologic factors, the possibility of chance or accident, which must always be taken into account, was seriously considered. In smaller series than the present, chance may have undoubtedly played a large part as it most probably has in a number of my own cases. Ultimate results will naturally vary within certain limits, depending upon special groups of sterility cases and upon the thoroughness with which treatment is carried out. The weight of evidence, all factors considered, points in the larger series of eventuating pregnancies to the fact that, by relieving tubal obstruction, uterotubal insufflation exerts a therapeutic influence in female sterility.

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SWEAT GLAND TUMORS OF THE VULVA, BENIGN (HIDRADENOMA) AND MALIGNANT (ADENOCARCINOMA)

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SWEAT gland tumors have been observed in various parts of the body, perhaps most often in the breast. They are rare, however, and there appears to be no crystallization of opinion among pathologists as to the interpretation of individual cases, or as to the histogenetic problems involved in this tumor group. A glance through any of our modern textbooks on pathology reveals that only a perfunctory and unsatisfying paragraph or two is likely to be devoted to the subject of sweat gland tumors.

The first instance of a tumor for which a sweat gland origin was assumed appears to have been that of Peterson[1] in 1893, the growth involving the skin over the sternal area, although in the case of a small bone tumor reported by Thierfelder[2] as far back as 1870 a sweat gland origin was at least suspected. Since both these tumors are reported to have contained skin elements, such as hair and sebaceous material, a sweat gland origin seems far less likely than that they were of dermoid nature. These cases, as well as many others, are reviewed by Pick[3] in his important contribution of 1904, to which frequent reference will be made in this paper. This author concluded that among the early cases in which a sweat gland origin was assumed only four appeared to be unquestioned. These were the tumors reported by Peterson[4] in 1892 (not the one alluded to above), Bartel[5] in 1900, Perthes[6] in 1903, and Schickele[7] in 1902.

The case of Schickele is of especial pertinence as regards the immediate subject of the present paper, because it is the only one of the above-mentioned group of four in which the tumor involved the vulva. Schickele's own interpretation of the growth was that it was of mesonephric origin, but a review of his report leaves no doubt as to the correctness of Pick's conclusion that the tumor belongs to the sweat gland group. To the four previously reported cases of genuine sweat gland tumors, Pick adds three of his own, in one of which the tumor was multiple. In all of these the lesions were located in the vulva.

As regards the sweat gland tumors of the vulva, there can be no doubt that these tumors were encountered long before any of the observations reported above, though the real nature of the lesion was either not suspected or at least not established. For example, it is quite certain that a vulvar tumor reported by Werth[8] as far back as 1878 was of this type, while in the tumor of the labium majus reported by Braun[9] in 1892 a sweat gland origin was actually suggested by the author, although this case was not in Pick's group of authentic early cases. Again, a very typical case is described by Gebhard[10] in his *Pathologische Anatomie des Weiblichen Sexualorgane* (1899), but the author expressed himself as totally at a loss as to its origin.

Pick's exhaustive paper established beyond doubt the sweat gland origin of certain vulvar lesions, and it included also an accurate description of the

histological characteristics of these growths. In his description Pick repeatedly stressed the double layer of cells present in some sweat glands, and also in the acini of these tumors. Again, he called attention to the layer of "ectodermal muscle cells" seen between the epithelium and the membrana propria of certain sweat glands, and also in every one of the vulvar tumors described by Pick. This myoepithelial layer had been described by von Koelliker[11] as far back as 1889. He mentioned, however, that not all of the sweat glands show these elements, and he quotes Rabl[12] as stating that certain sweat glands in the axillary and scalp areas show three or even four layers of epithelial cells. Moreover, he calls attention to the fact that Perthes in the description of his case noted that secretory products, not merely degenerative, were found in some gland lumina.

Types of Sweat Glands.—These facts are noted simply because they indicate a growing realization of the fact that sweat glands are not all alike histologically, and probably not embryologically or functionally as well. The sweat glands were first described by Purkinje in 1833, the sebaceous glands by Eichhorn some years earlier, in 1826. Even at the present day, it is quite certain that the prevalent concept of the skin glands is that they are quite sharply divisible into these two groups, the acinous sebaceous glands secreting the characteristic sebaceous material and the tubular sweat glands the watery sweat. This, however, is not the case, for all sorts of intergrades have been noted, both histological and functional. In 1879 Graff[13] showed that the secretion of certain of the tubular glands contains fatty material, while Ranvier[14] described the presence of desquamated gland cells in the secretion of certain glands. A thorough review of these and many other similar observations is given by Hoepke,[15] to whose article the interested reader may be referred.

On the basis of such observations, we can no longer think of the sweat glands as having a stereotyped structure or function, and they can now be subdivided into several varieties. Various groupings were described by the early workers in this field, such as Schiefferdecker[16] and Schaeffer.[17] However, the simplest and most serviceable subdivision would appear to be into three groups, as given by Maximoff.[18] Those in which the epithelial gland cells remain intact during the secretory process are designated as merocrine glands. Those in which the secretion includes extruded portions of the cytoplasm of the cells are spoken of as the apocrine glands, and their distribution appears to be limited to certain areas of the body. These include the axillae, the nipple area, the mons pubis, the abdominal walls, the groins, the labia majora, and the perineum (Hoepke). They are always associated with hair follicles. This is of interest, since the sebaceous glands, perhaps more traditionally associated with the hair follicles, are also found in hair-free regions of the body, such as the labia minora, the glans and prepuce, the oral cavity and lips (Hoepke).

A third group of glands is the holocrine, in which the lining epithelial cells degenerate completely and make up the gland secretion, as in the case of the sebaceous and mammary glands. None of the ordinary sweat glands of the body, however, are of this type.

From what has already been said, as well as from other observations which could be adduced, there is ample justification for the statement, previously made, that all sorts of histological and functional gradations are to be noted in the sweat glands, and the question arises as to whether any of these varieties is more prone to neoplastic growth than others.

We know of no data on this point as applied to sweat gland tumors of other parts of the body, but as regards the vulva there is some evidence to indicate that it is the apocrine group of glands which are most likely to give origin to the sweat gland tumors of this region. With some reported cases the assumption of such an origin seems justified, with others not so clear, and it is probable that the assumption of an apocrine gland origin for practically all these tumors has been overaccentuated. It was apparently McDonald[19] who suggested this explanation, and it undoubtedly applies to some cases. However, the structure of different sweat gland tumors of the vulva shows considerable variation, and the classical original paper of Pick took cognizance of these variations in structure.

Types of Benign Sweat Gland Tumors.—Pick set forth also a nomenclature based on variations in histogenesis. He applied the designation of hidradenoma to those tumors which arise from mature sweat glands, and that of adenoma hidradenoides to those which arise from immature or undifferentiated sweat glands, or from the surface epithelium itself. The latter concept is in line with the view of Krompecher[20] that the basal cells of the skin epithelium may give rise to either sebaceous or sweat gland tumors, although not all dermatological pathologists accept this view. Pick described also a third variety characterized by marked papilliferous tendencies, and to this he applies the designation of hidrocystadenoma papilliferum. Moreover, Meyer[21] has called attention to the fact that in some vulvar lesions one deals merely with adenoma-like proliferations of the sweat glands rather than with genuine adenoma. Our Case 11 appears to belong to this category.

All these subdivisions are confusing. In some tumors the histological study will probably justify one or other of the designations mentioned above, but in others there is sure to be uncertainty on this point. It is probable that the average gynecologic pathologist will prefer to include all genuine sweat gland adenomas, regardless of precise mechanisms of histogenesis, as hidradenoma. There would seem to be no objection to this, since the term hidradenoma is a fairly inclusive one, embracing all adenomatous tumors of sweat gland origin.

Similar uncertainty must often exist as to whether or not the tumor arises from apocrine glands. Circumstantial but not conclusive evidence may be furnished by the presence of apocrine glands adjoining the lesion. However, it is not always easy for the gynecologic pathologist, inexperienced as he is likely to be in these dermatological niceties, to differentiate the apocrine from the merocrine glands, especially since intermediary histological types exist. The former are apt to be somewhat larger and less tortuous, the myoepithelial layer is apt to be more highly developed, and the epithelial cells may show the protrusions which precede the cytoplasmic extrusion, while cast-off

Fig. 1.—Apocrine gland "pad" from axilla of gorilla. Note, especially near the center, the rather streaky appearance produced by tangential section through the myoepithelial layer. (Courtesy of Dr. W. T. Strauss, Carnegie Institute of Embryology.)

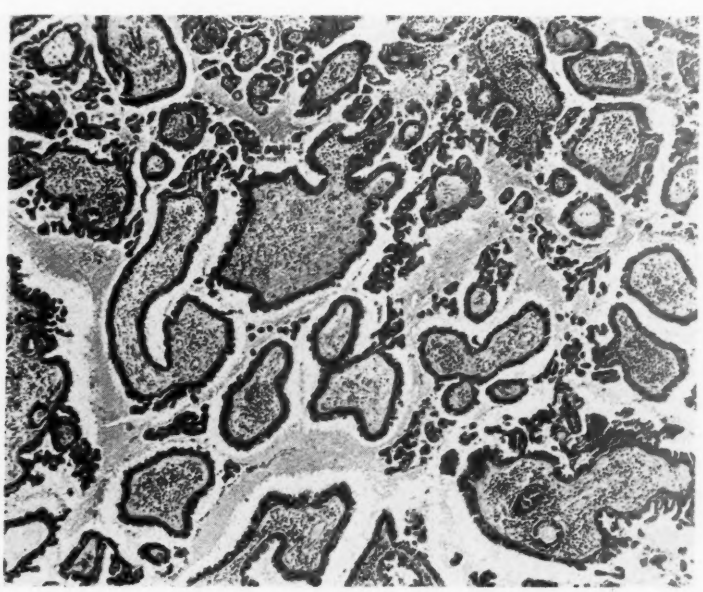

Fig. 2.—A sweat-gland tumor from the scalp, showing the double epithelial layer so often found in sweat gland tumors. The pale tuft-like appearance of the epithelium, seen especially in the upper portion of the section, suggests an apocrine origin.

cytoplasmic and at times nuclear material may be found within the lumina. The epithelial layer has a tendency to draw away from the basement membrane. There are other differences which have been described, but the distinction is not always easy. Dr. Wm. T. Strauss of the Carnegie Institute tells us that, in primates like the gorilla, large collections of apocrine glands, or apocrine "pads" occur in the axilla as well as in certain other areas. (Figs. 1 and 2.)

Clinical Characteristics.—Hidradenoma of the vulva has been noted at various age periods, but not, so far as we know, in very young individuals. The

Fig. 3.—Case 1. (Gyn. Path. 2863.) A small vulvar nodule in the fold between the left labium minus and majus, in a patient of 40 years. The section is a poor one, dating from the early days of the laboratory (Oct. 13, 1898).

Fig. 4.—Case 2. (Gyn. Path. 10525.) A nodule from the right labium majus, showing a typical intracystic papillary structure. The glands in the wall appear to be of merocrine rather than apocrine type.

youngest patient in our series was 28 years, the oldest 67 years. The most common location of the lesion is on the labia majora, and next most common in the paralabial skin or perineum. In a few cases, as in one of our own, one of Schickele, and one of Eichenberg,[22] the growth has been situated on the

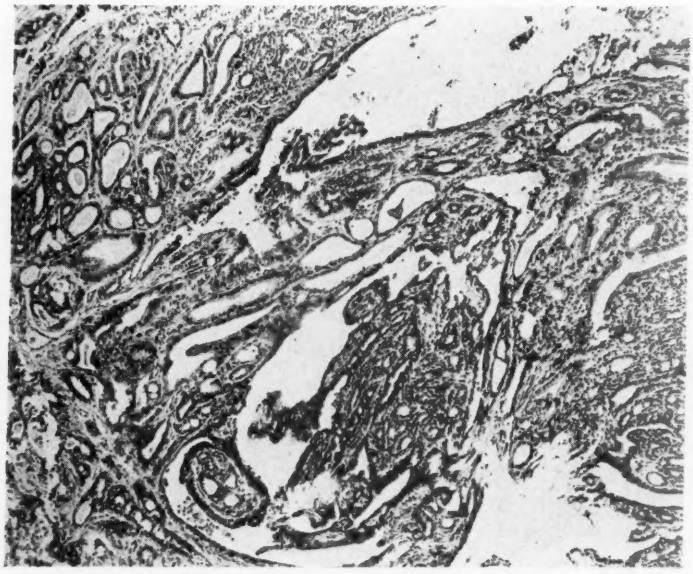

Fig. 5.—Case 3. (Gyn. Path. 42177.) A small, well-encapsulated nodule from the labium minus of a patient of 67 years. Its diameter was 1 cm. Most of the glands suggest the apocrine type. Removed incidentally to plastic operation. (Private patient of Dr. Emil Novak.)

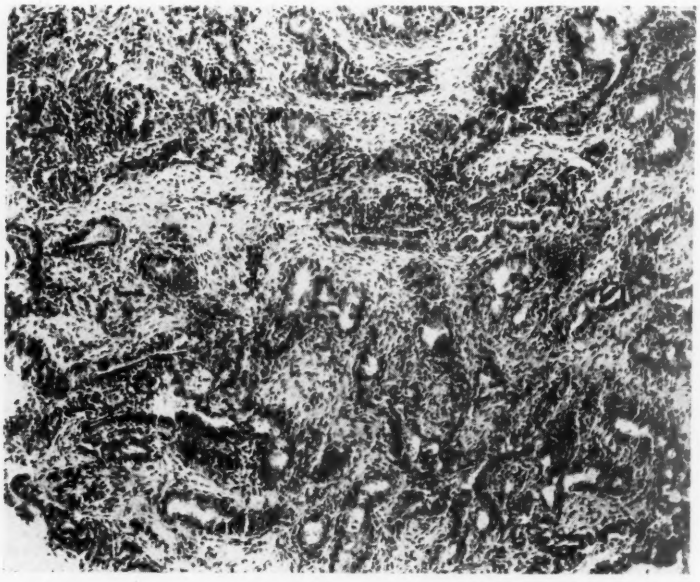

Fig. 6.—Case 4. (Gyn. Path. 44563.) The tumor formed a small nodule in the right labium majus. The patient, age 36, was pregnant at 3 months. Because of apprehensiveness as to possible malignancy, the right inguinal glands were excised, but no metastasis found, and the patient remained well. (Private patient of Dr. E. H. Richardson.)

labium minus. This is of interest since many histologists believe that sweat glands are not normally found in the lesser labia. This may be true of the ordinary sweat glands, but one cannot be so sure as to glands of the apocrine type, which are rather closely related to sebaceous glands, of which there are

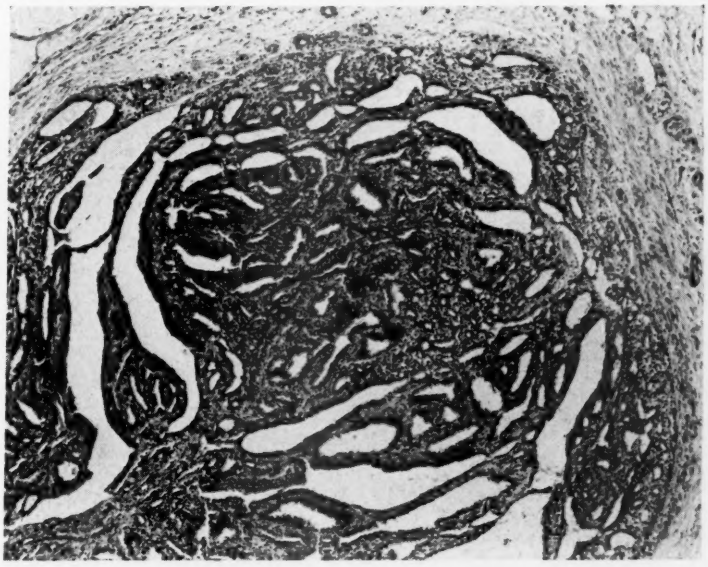

Fig. 7.—Case 5. (Gyn. Path. 45958.) A nodule from the left labium minus in a patient of 37 years. (Private patient of Dr. H. S. Everett.)

Fig. 8.—Case 6. (Gyn. Path. 47180.) A nodule the size of a cherry in left labium minus, resembling a fibroma, but with rather reddish hue to the overlying skin. The patient was 55 years of age. The picture in this case is that of a loosely adenomatous growth, with superficial ulceration of the overlying skin. (Private patient of Dr. Emil Novak.)

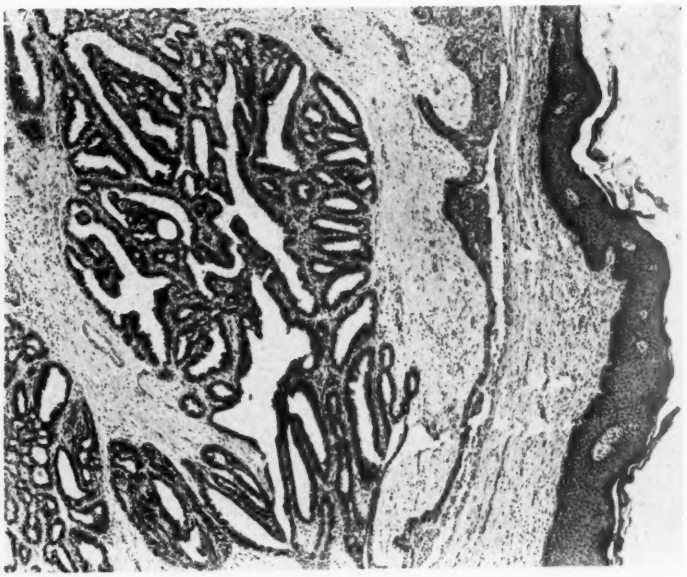

Fig. 9.—Case 7. (Gyn. Path. 51053.) A nodule 1½ cm. in diameter in left labium majus. Patient was 37 years of age. Note the stratification of the epithelium just below the skin. (Private patient of Dr. Emil Novak.)

Fig. 10.—Case 8. (Gyn. Path. 54045.) A small vulvar nodule from a patient of 39 years. The glands in the vicinity of the nodule are not of apocrine type. (Private patient of Dr. Leo Brady.)

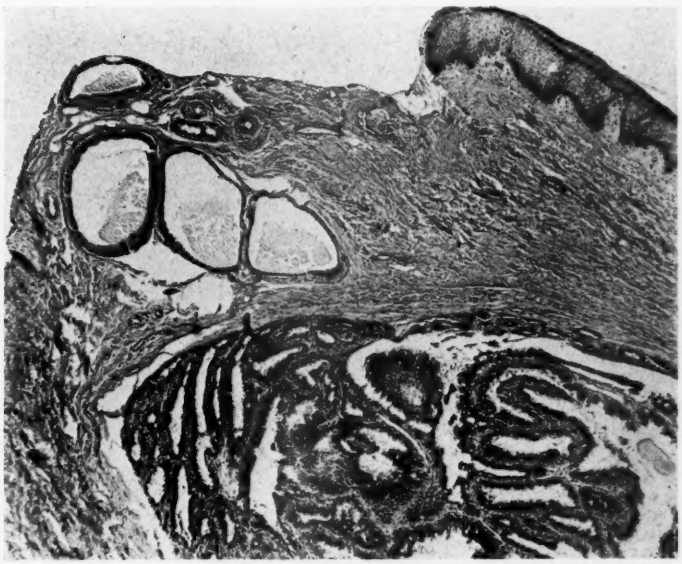

Fig. 11.—Case 9. (Gyn. Path. 56523.) A small cystic nodule in labium majus, from a patient of 28 years. Just above the hidradenoma can be seen a large dilated apocrine gland. (Private patient of Dr. H. S. Everett.)

Fig. 12.—Lower-power of another section from Case 9, showing the extrusion of the papillary growth through the skin defect.

Fig. 13.—Case 10. (Gyn. Path. 58078.) A small, subcutaneous vulvar nodule in a patient of 52 years. The adjacent glands do not appear to be of apocrine type. (Private patient of Dr. L. R. Wharton.)

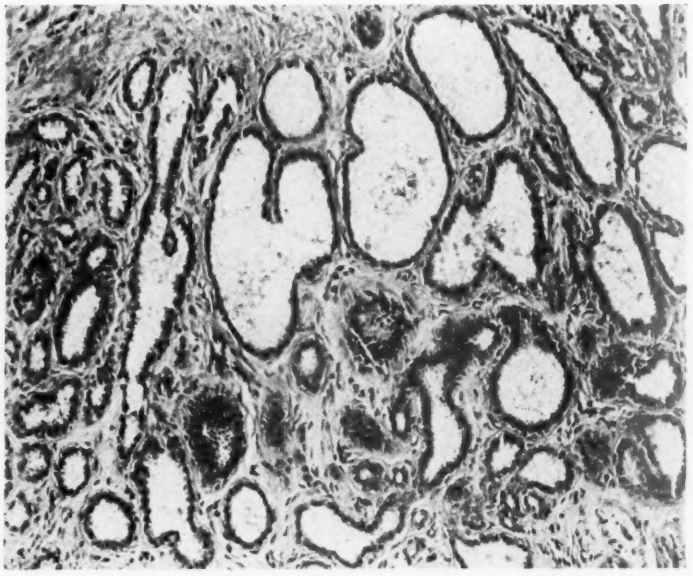

Fig. 14.—Case 11. (Gyn. Path. 60943.) A nodule appearing clinically like a small fibroma in a patient of 46 years. The structure is not like that of a typical hidradenoma, suggesting simply a hyperplastic increase of apocrine glands. Since it formed a definite neoplastic nodule, the case has been included as a benign sweat gland tumor. (Private patient of Dr. Leo Brady.)

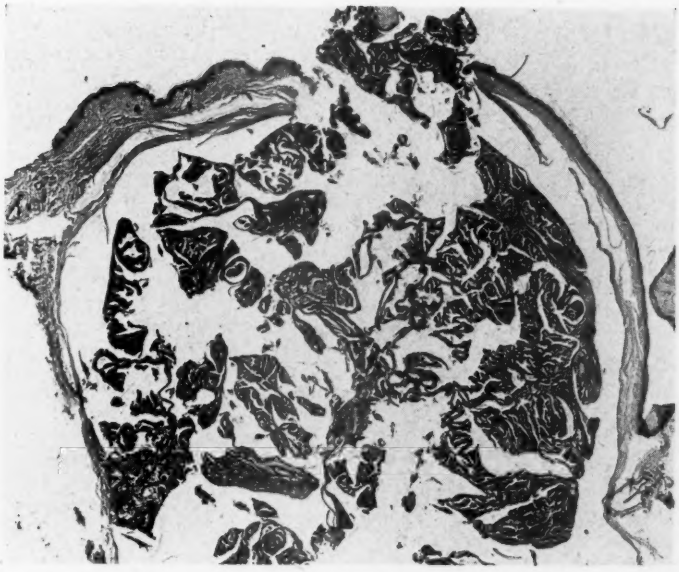

Fig. 15.—Case 12. (Gyn. Path. 66068.) A small reddish nodule on the left labium minus, in a patient of 61 years. Pressure over nodule caused exudate of pulpy, reddish-brown material. The section shows the intracystic papillary pattern seen in many hidradenomas, and also the extrusion of papillary material through the skin opening. (Private patient of Dr. Emil Novak.)

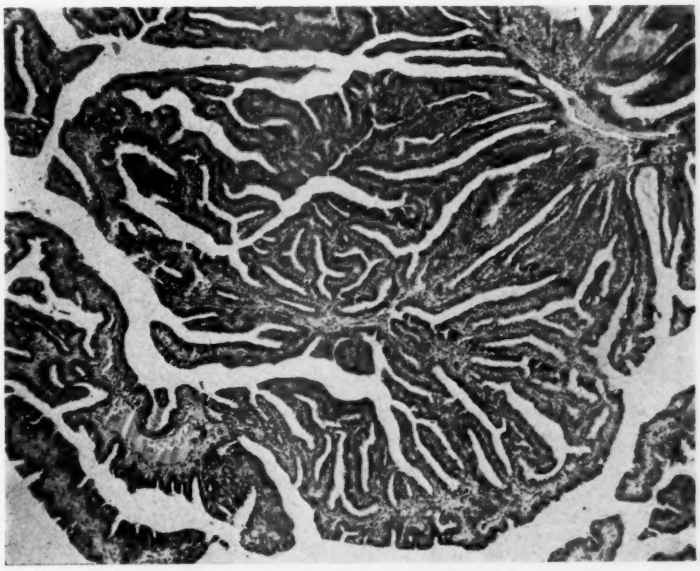

Fig. 16.—Case 13. (Gyn. Path. 62373.) A small rounded sessile nodule 1 cm. in diameter in the vestibule, 1 cm. to right of midline and 1½ cm. posterior to the glans clitoridis. No other hidradenoma has been reported as situated in the vestibular area. The patient was 45 years of age. (Private patient of Dr. Emil Novak.)

enormous numbers in the labia minora. There appears to be no precise knowledge on this point, and perhaps the sweat glands from which hidradenoma develops in this region are to be interpreted as aberrant or misplaced.

In our most recent case, observed in a private patient of the senior author, the location of the tumor was in the anterior position of the vestibule, about 1 cm. to the right, and 1½ cm. anterior to the glans clitoridis. So far as we know, no other hidradenoma has been observed in this region, and yet it was quite typical, as can be seen from Fig. 16. Clinically, it presented as a raised, sessile, rounded nodule, 1 cm. in diameter, with a tiny abrasion-like reddish area at its summit, so that a presumptive diagnosis of hidradenoma was made before excision of the nodule.

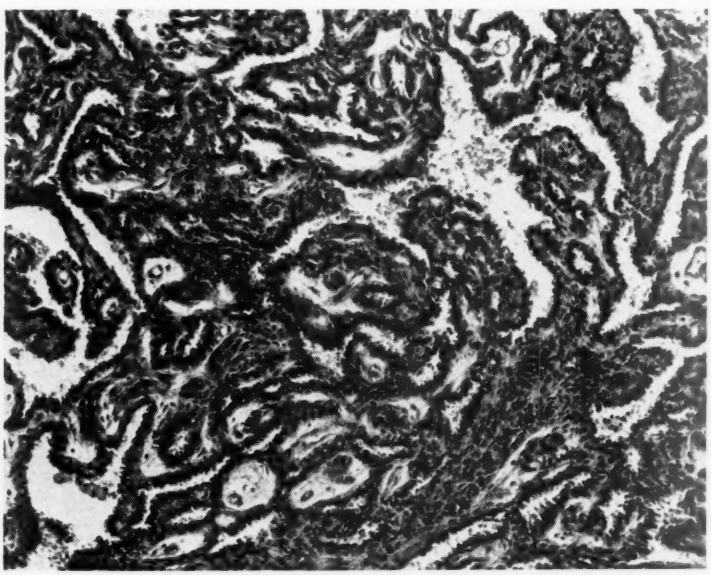

Fig. 17.—Case 14. (Gyn. Path. 62662.) A nodule 2 cm. in diameter, slightly elevated, in perineal body just behind right labium majus (see Fig. 18). (Private patient of Dr. R. W. Te Linde.)

It is of interest to note that all of our fifteen cases of hidradenoma occurred in white patients, and not a single one in Negro women, in spite of the fact that such a large proportion of our clinic patients are Negroes. This is all the more surprising since Homma[23] has shown that the apocrine glands, which have been thought to be the common source of hidradenomas, are three times as numerous in Negroes as in whites.

The gross appearance of the lesion varies. It is always small, rarely reaching a size larger than that of a cherry, and usually not over 1 cm. in diameter. It may present as a small, firm, subcutaneous nodule, like a small skin fibroma, covered by intact skin. In other cases it is soft, resembling a small sebaceous cyst, for which it is commonly mistaken. Not infrequently there is a small superficial granular area on the surface. If pressure is made on the small nodule, one is apt to be surprised by the fact that, instead of a

typical sebaceous exudate, the material expressed is reddish-brown and pulpy. This should at once suggest the real nature of the lesion. There is no pain, and often no tenderness or soreness, especially when the skin surface is intact, and the nodule is ordinarily quite movable. In a considerable number of cases the patient herself has not noticed the nodule, its removal being incidental to vaginal operative procedures.

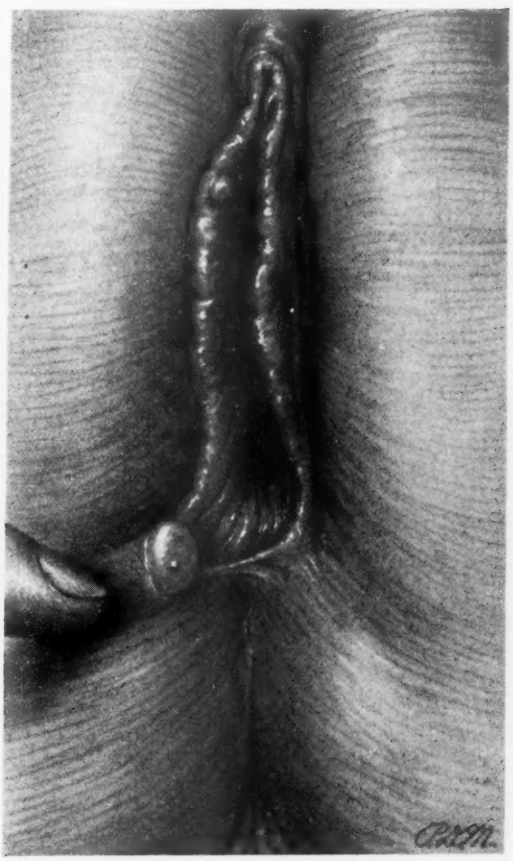

Fig. 18.—Gross appearance in Case 14. (Kindness of Dr. R. W. Te Linde, from forthcoming book on *Operative Gynecology*.)

Microscopic Characteristics.—There is considerable variation in the microscopic appearance of these hidradenomas, as might be inferred from what has already been said. In the most common variety, the pattern is of intricate adenomatous type, some of the glands being small and closely packed, others large and cystic. The epithelium in many, but not by any means all of the glands, shows an inner short columnar or cuboidal layer, and beneath this a layer of the rather closely packed small dark nuclei of the myoepithelium. The latter, however, is frequently absent.

On the other hand, there is a frequent tendency to proliferation and stratification of the epithelium, so that some of the smaller lumina may be com-

pletely filled. Even patches of pavement epithelium may be seen, not unlike the squamous plaques seen in cervical epidermidization, and Schiffmann[24] described small epithelial pearls which he thought might indicate malignancy. These epithelial proliferative changes might well in other locations lead to this suspicion, but they are much less significant in these sweat gland tumors which are essentially normal in appearance, and these may be of either the merocrine or apocrine types. In a number of our own cases, collections of essentially normal glands, often clearly of apocrine variety, are seen side by side with areas of involved tubular pattern in which the sharply defined epithelium is strikingly different from the rather large pale cells, with small nuclei, which line the apocrine glands. It seems a fair assumption that such tumors are not of apocrine gland origin, but, on the other hand, such pictures would suggest also that the epithelium of the tumor may undergo a considerable degree of transformation or dedifferentiation. In other tumors the original apocrine epithelial characteristics seem to be retained, so that even in areas where there has been much proliferation, the tufts of epithelium often produced may be composed of the large, pale, and perhaps indistinctly marked epithelial cells suggestive of apocrine histogenesis.

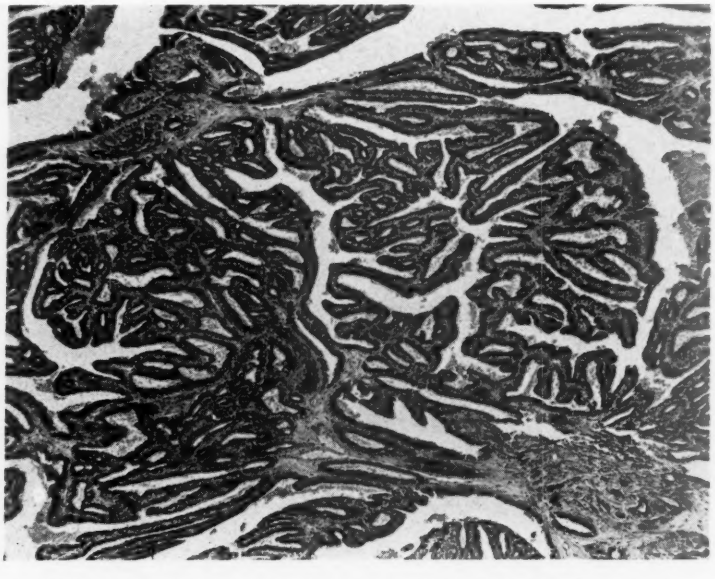

Fig. 19.—Case 15. (Gyn. Path. 62960.) A small, reddish-purple growth from the left labium, just anterior to the position of Bartholin's gland. Patient was 47 years of age. (Private patient of Dr. Leo Brady.)

In other tumors the tubules are small and narrow, arranged in a zigzag fashion, and all lined by low, sharply differentiated epithelium, with perhaps sweat glands of the ordinary nonapocrine variety in the vicinity. In such cases it would seem farfetched and probably incorrect to invoke an apocrine gland origin. We cannot insist on any of these finer distinctions, but it does seem to us that the available evidence does not justify the assumption that hidradenoma is always of apocrine gland origin.

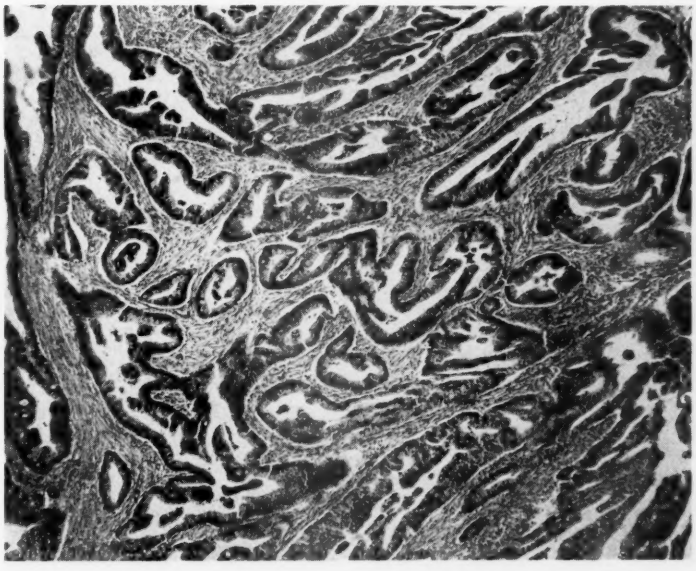

Fig. 20.—Case 16. (Gyn. Path. 33437.) Apparently primary adenocarcinoma of vulva, the lesion involving almost the whole vulva, but not Bartholin glands. The patient was 60 years of age. There was no evidence of any other possibly primary site. Treatment was palliative and the patient died about two months after being seen. A sweat gland origin is possible, but cannot be assumed.

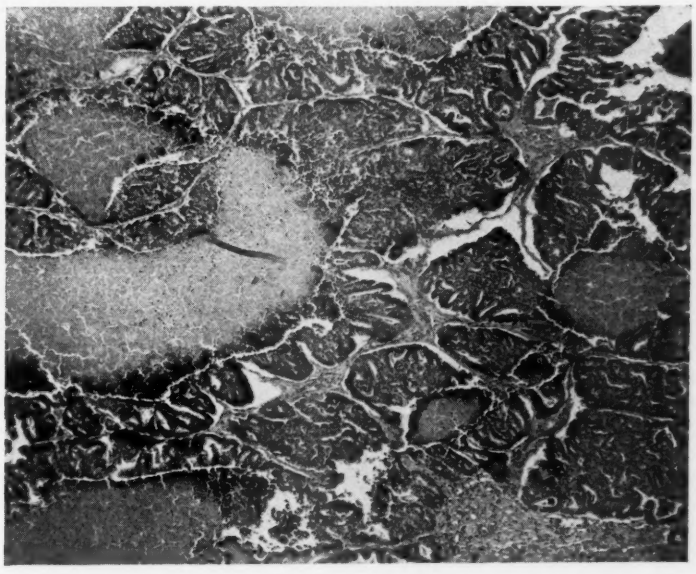

Fig. 21.—Case 17. (Gyn. Path. 33613.) Another apparently primary and highly undifferentiated adenocarcinoma of vulva, presenting as a large, indurated, ulcerative lesion of the posterior part of the left labium majus, in a patient of 41 years. A radical operation was done, but the patient died one year after operation. Here again a sweat gland origin is possible, but not by any means certain.

The Question of Malignancy.—From what has been said as to the microscopic pictures presented by these sweat gland tumors, it is easy to see how they can be readily mistaken for adenocarcinomas. This would apply especially to the highly papilliferous variety. Such an error in diagnosis would be natural enough if one did not know the source of the lesion. For example, Aschheim[25] mentions a case in which he examined sections of what he thought was a biopsied cervix, and in which he made a diagnosis of adenocarcinoma. He learned later that the lesion was from the vulva, and revised his diagnosis to that of benign hidradenoma. He agrees that hidradenoma is to be looked upon as benign, and expresses doubt as to the supposed malignancy in the case of Ruge, which will be mentioned in the next paragraph.

Throughout the entire literature of the subject there is constant emphasis on the absence of any suggestion of clinical malignancy, and also constant reference to one or more of four cases in the literature which have been reported as malignant. We have carefully reviewed the original reports of these four cases, and conclude that in only one of them does there seem to be valid evidence for the assumption of malignancy. The first of this group was reported by Ruge[26] in 1905 under the designation of "Schweissdrüsenkarzinoma." The histological description and the illustrations depict a tumor identical with all the other benign hidradenomas which have been reported, and there is nothing in the report to suggest clinical malignancy of the lesion which was cured by simple excision.

The sweat gland epithelium appears to be prone to this rather pleomorphic proliferative activity. Mitoses, on the other hand, are seen only infrequently.

Even in cases in which the pattern is highly pseudomalignant, one not infrequently finds areas of sweat glands.

The second case which has been quoted by various authors as possibly malignant is that of Schiffmann,[24] in 1920. This likewise was a clinically benign nodule of the labium majus observed in a patient 40 years of age, and treated by simple excision. In the microscopic description Schiffmann mentioned that in addition to the usual features a number of small epithelial pearls were seen in certain areas, although otherwise the tumor was typical enough. He rather naively suggests that the term adenoma malignum might be applied to lesions in which the pathologist is in doubt as to whether they are benign or malignant. He compromises by calling his tumor an adenocancroid. However, it was clinically benign and resembles many of the other clinically benign cases reported except for the so-called pearls. The latter, however, are not to be considered as suggesting malignancy, for reasons which have been already discussed.

Another case sometimes quoted is that of Burg[27] (1930), but a reading of his paper shows that he considered it to be clearly benign, classifying it as adenoma hidradenoides. For that matter he expressed doubt as to the supposed histological malignancy of the cases of Ruge and Schiffmann. So far as we can see, the only reason that some authors have included this case in the supposedly malignant group is Burg's remark that the material expressed from the nodule before excision had led him to suspect possible malignancy.

Finally, reference must be made to the paper of Eichenberg[22] (1934), from material studied in the laboratory of Robert Meyer. Twelve cases of typical hidradenoma were reported, all cured by excision. In one of these, a small local recurrence was noted, requiring further excision, but this Eichenberg himself says was obviously due to the incompleteness of the first excision.

In the course of his paper, however, Eichenberg mentions another case of vulvar tumor, also thought to be definitely of sweat gland origin, in which the histological picture was quite different. Unfortunately, there are no illustrations of the microscopic appearance, but the author emphasizes the extreme degree of epithelial proliferation and the invasion of surrounding tissue by cell columns and tubules. Meyer interpreted this tumor as an adenocarcinoma arising secondarily in a hidradenoma. As to its clinical malignancy, there is little doubt. It was described as an almond-sized nodule in the left labium majus, which was widely extirpated with the growth, together with the left inguinal glands, which showed definite metastasis. There had been no recurrence two years after operation.

It will thus be seen that only a single case in the literature can be properly considered as malignant from a clinical standpoint. It is surprising therefore that Folsome,[28] so recently as 1940, stated that 27 per cent of cases were locally invasive and presumably malignant, and we cannot imagine the basis for this statement.

Even more unfortunate is the fact that in a very recent report, that of McDonald, Lovelady and Waugh,[29] a large group of vulvar sweat gland tumors is reported under the designation of adenocarcinoma of the vulva. Thirty of these, on the basis of the clinical and histological description and the accompanying illustrations, belong to the benign hidradenoma group. The other two appear to be malignant tumors of unknown histogenesis, nothing in the descriptions suggesting that they are of sweat gland origin, although this possibility cannot be ruled out. With reference to the larger group of thirty sweat gland tumors, the authors emphasize their clinically benign nature, stating that in every instance simple excision effected cure. In other words their designation of the tumors as papillary adenocarcinomas was based entirely upon their interpretation of the local histology.

Granting the superficial resemblance of some hidradenomas to adenocarcinoma, the illustrations accompanying this paper leave no doubt as to the hidradenomatous nature of the depicted lesions and would not seem to justify even a histological diagnosis of adenocarcinoma, if one is familiar with the frequent stratification and the frequent papilliferous ingrowths which characterize clinically benign tumors of sweat glands in this region. The term adenocarcinoma certainly conveys the idea of clinical malignancy, and it would seem incredible, if the tumors were really adenocarcinomas, that clinical malignancy and metastasis would not have been observed in at least some of this rather large group of cases. This is especially true in view of the strong propensity of vulvar carcinoma in general to metastasize rather early in its course. In view of these facts, we believe that a disservice has been done by these authors in thus flat-footedly designating these tumors as adenocarcinomas.

This is not to say that genuine adenocarcinoma cannot have a sweat gland origin, as would seem to be attested by the case of Eichenberg,[22] described above. Even in the latter, the histological picture differs from that of the papilliferous but clinically benign hidradenomas only in degree. Epithelial proliferation even in the latter may be pronounced and plaques of horny epithelium may be seen, producing pictures which, in other organs like the uterus or ovary, would incline one to the diagnosis of malignancy.

The practical lesson, on the basis of all past experience with these vulvar growths, is that such histological features often characterize entirely benign lesions of sweat gland origin, but that, in spite of this fact, one should not treat these growths too lightly. When they are small and slow growing or quiescent, as practically all reported cases have been, simple but complete excision suffices to effect cure. It is always advisable, however, especially in the case of lesions showing a high degree of epithelial proliferation and a markedly papilliferous pattern, to keep the patients under observation. This seems like a wise precaution in spite of the fact that in only one case in the literature has malignancy appeared to develop in a hidradenoma. Even this assumption may not be correct, as the tumor may have been definitely malignant from the beginning. In other words, the sweat glands may be the seat of origin of adenocarcinoma just as they may be of the benign hidradenoma, and not necessarily with the intermediation of the latter.

Possible Sweat Gland Origin of Some Primary Vulvar Adenocarcinomas.—Primary adenocarcinoma of the vulva is exceedingly rare, and when it does occur, one can usually do little more than speculate as to its origin. From this statement we can perhaps except carcinoma of Bartholin's gland, as the location of the tumor in such cases will usually be helpful in indicating its source. Other possible sources would be vestigial mesonephric (Wolffian) structures, vulvar endometriosis, and aberrant breast tissue, of which a number of cases have been reported. In addition to these, one must also think of the possibility of sweat gland origin. We have observed two instances of primary adenocarcinoma in which a sweat gland origin was thought to be probable, but certainly not established beyond doubt (Figs. 20 and 21). Other cases of this "probable" type have been reported by McDonald and his coworkers,[29] but the fact remains that this is still a rather vaguely defined entity.

Instead of giving detailed reports of the fifteen cases of hidradenoma which we have observed, the essential data are included in the self-explanatory legends of the photomicrographs of each of these tumors. We may simply add that all these tumors were treated by simple excision, and no recurrence was noted in any case.

Summary

The sweat gland tumors of the vulva constitute a relatively rare but highly interesting group. Clinically they present as small and innocent-looking growths on or near the vulva, but to one not familiar with their histological appearance the microscopic picture is apt to be rather startling, and perhaps to lead to the diagnosis of adenocarcinoma. However, in only one case in the litera-

ture, that of Eichenberg, has there been apparently unimpeachable evidence of malignant change, both clinical and microscopic. All other cases, including the fifteen cases reported herewith, have been clinically benign and all have been cured by simple excision.

Granted that the characteristic microscopic picture of these growths might well in other tissues lead to the diagnosis of adenocarcinoma, there would seem to be no justification for applying the term adenocarcinoma to these notoriously benign sweat gland tumors. It is entirely possible, and perhaps even probable, that some instances of the rare primary adenocarcinoma of the vulva may be of sweat gland origin, as in the two cases of this group we have included in this paper. Such an origin, however, is difficult to establish. The histogenesis of these sweat gland tumors has been thoroughly discussed in our paper, and the suggestion made that the apocrine gland derivation of these growths has probably been overaccentuated, though our knowledge on this point is still very incomplete. The clinical and microscopic characteristics of hidradenoma have likewise been rather fully discussed in the paper.

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TEN YEARS OF CESAREAN SECTION AT THE BOSTON LYING-IN HOSPITAL*

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THIS report covers the 1,887 consecutive cesarean sections performed at the Boston Lying-In Hospital during the ten years from 1934 to 1943 inclusive. One thousand ninety-four, or 58 per cent of these operations, were on patients admitted to the public wards; 793, or 42 per cent, were on private patients. All public ward patients are on the teaching service of Harvard Medical School, and those delivered by cesarean section were operated on by the visiting obstetricians, the resident obstetricians, and the house-officers; such patients are under the direction of the chief of staff of the hospital, and the policies governing their treatment are determined by him in consultation with the other members of the visiting staff. Operations on the private patients are performed by the visiting staff and by the courtesy staff, which consists of selected graduates of the Boston Lying-In Hospital. Policies governing the treatment of private patients are left largely to the individual obstetricians.

Fig. 1 compares the results obtained during this ten-year period with cesarean section after viability and with methods of pelvic delivery in the case of the public ward patients only, who were selected because their records were readily available. This chart shows: (1) Normal delivery was fifteen times safer for the mother than cesarean section and over two and one-half times safer for the infant. (2) Low forceps were seven and one-half times safer for the mother than cesarean section and just as safe for the infant as normal delivery. (3) Other things being equal, cesarean section is not a substitute for either low-forceps or normal delivery. (4) On the other hand, midforceps was almost as dangerous for the mother as cesarean section and about eight times more dangerous for the infant. (5) Provided it is indicated, therefore, cesarean section compares favorably with midforceps as a method of delivery.

In studying these 1,887 cesarean sections, four questions are raised: (1) Was this operation employed too frequently, i.e., was it substituted for either normal delivery or low forceps in cases where either of these simple methods of delivery might have been employed? (2) What were the causes of maternal and fetal deaths in cesarean section? Might some of these deaths been avoided, and if so, how? (3) How did the results with private and public patients compare? (4) How did they compare with those reported in other series of similar magnitude? These questions may be answered by considering the following topics: (1) incidence; (2) the operators; (3) indications; (4) special diagnostic

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and therapeutic measures; (5) morbidity; (6) fetal mortality; (7) maternal mortality; (8) cesarean section as a method of delivery in certain complications of pregnancy and labor other than dystocia.

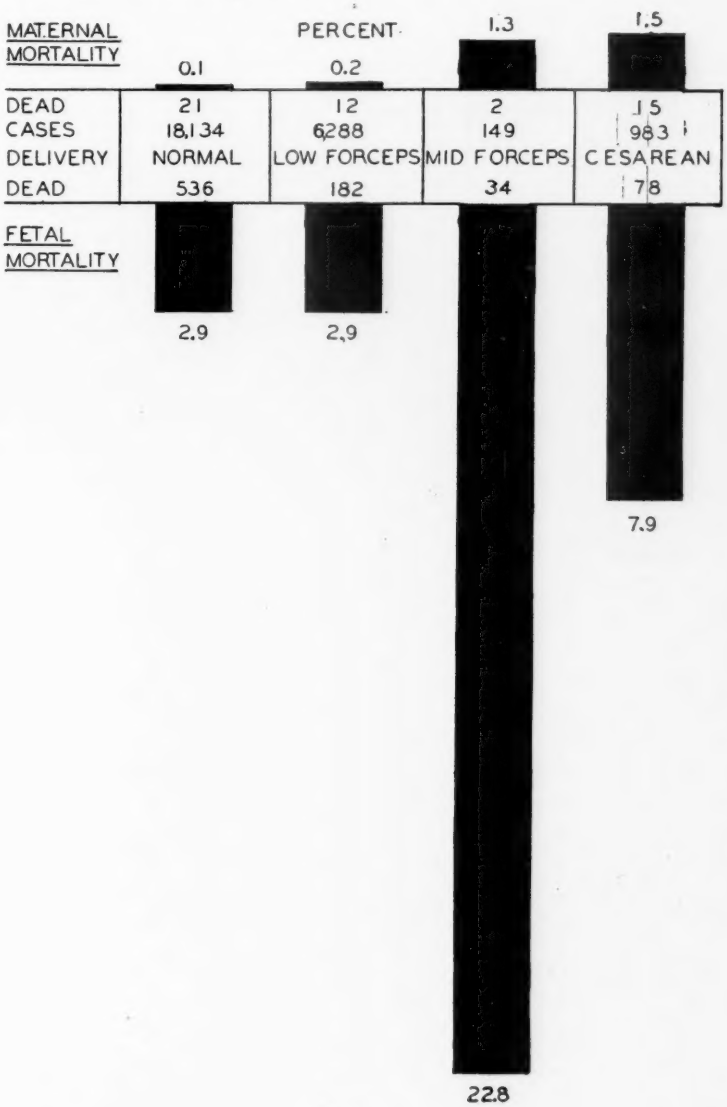

Fig. 1.

Incidence.—Fig. 2 shows the relative frequency with which cesarean section was employed during the ten years under study. It was performed relatively more than twice as often on private patients as on public ward patients. When this ten-year interval was divided into two periods of five years, each embracing approximately the same number of cesareans—almost a thousand, it is evident that although the total frequency had not changed much the individual fre-

quency was less during the last five years in both parts of the hospital. Comparative percentages from other sources show an incidence of 6.1 per cent for the Cleveland Maternity Hospital,[1] 5.5 per cent for the Chicago Lying-In Hospital,[2] 3.9 per cent for the Methodist Episcopal Hospital of Brooklyn,[3] 3.3 per cent for the State of Massachusetts,[4] and 2.5 per cent for the City of Philadelphia in 1941.[5] The total incidence at the Boston Lying-In Hospital during the ten-year period was 4.2 per cent, or one cesarean in every 24 deliveries; but this frequency was due to the relatively large number of cesarean sections performed on private patients. For the ten-year period, this was 6.7 per cent, or one in every 14 deliveries, a frequency higher than was reported from any of the sources quoted. Practically all the private patients were under the care of their

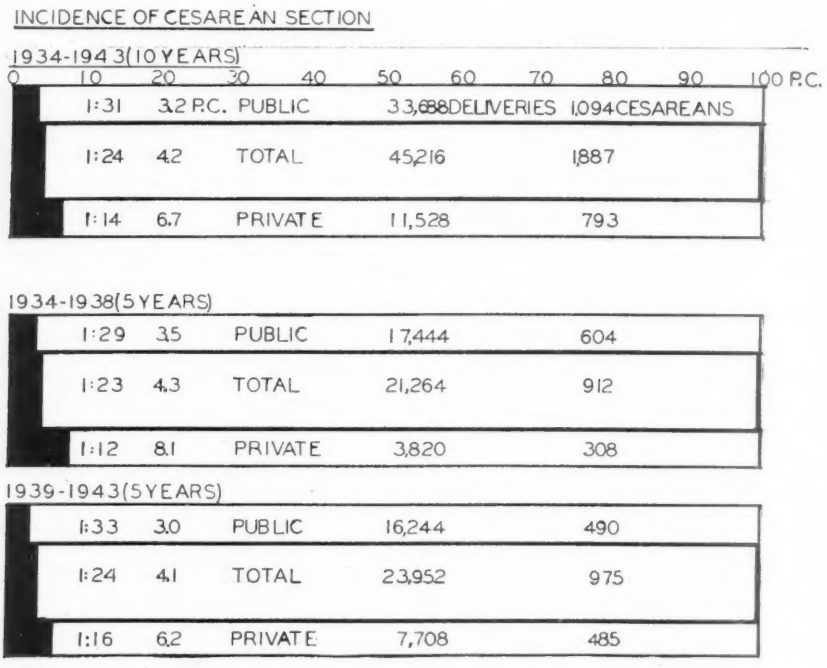

Fig. 2.

obstetricians throughout pregnancy, and few were referred to them as consultants because of obstetric abnormalities. On the other hand, a large number of the public ward patients were referred to the hospital from Boston and neighboring parts of New England because they suffered from complications. No patient is refused admission. In such a group one would expect a higher incidence of cesarean sections, but the reverse proved true. One cannot escape the suspicion, therefore, that a number of the private cases of cesarean section might have been delivered by simple pelvic means if the accoucheurs had possessed a higher degree of patience. On the other hand, an incidence of 3.2 per cent, or 1 in 31, for the public ward cases is well in line with the frequencies quoted for other hospitals and is almost exactly the same as that for the State

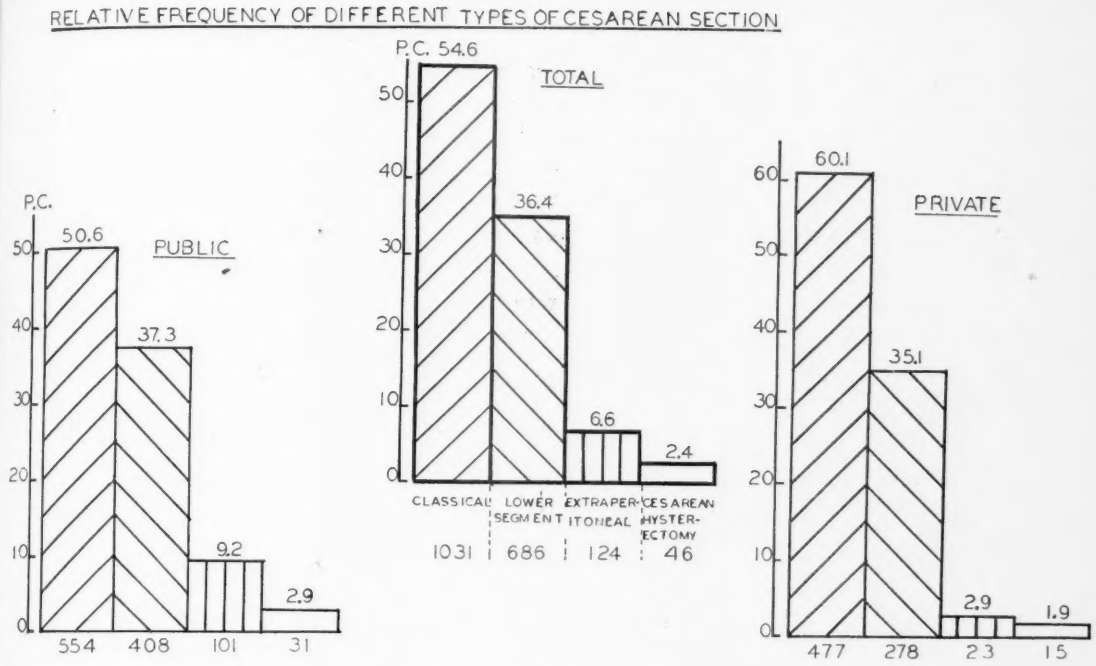
RELATIVE FREQUENCY OF DIFFERENT TYPES OF CESAREAN SECTION
P.C.
50.6
PUBLIC
37.3
9.2
2.9
554
408
101
31
P.C. 54.6
TOTAL
36.4
6.6
2.4
CLASSICAL
LOWER SEGMENT
EXTRAPERITONEAL
CESAREAN HYSTERECTOMY
1031
686
124
46
60.1
PRIVATE
35.1
2.9
1.9
477
278
23
15

Fig. 3.

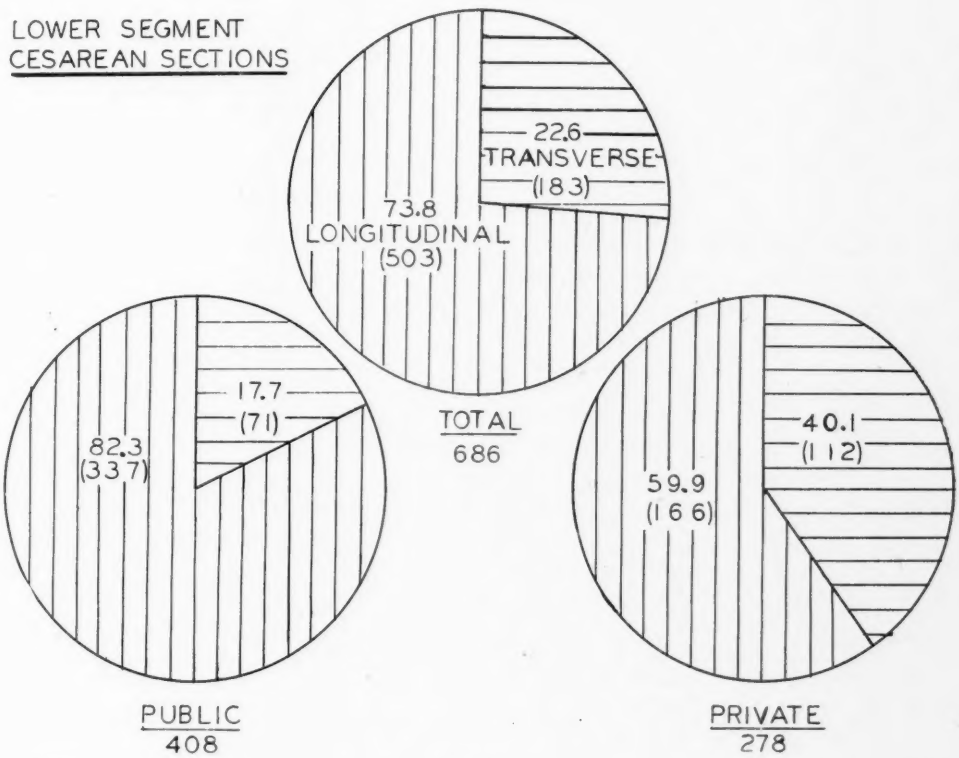
LOWER SEGMENT CESAREAN SECTIONS
22.6
TRANSVERSE
(183)
73.8
LONGITUDINAL
(503)
TOTAL
686
17.7
(71)
82.3
(337)
PUBLIC
408
40.1
(112)
59.9
(166)
PRIVATE
278

Fig. 4.

of Massachusetts. Fig. 1 also indicates that there were relatively fewer cesarean sections performed in both parts of the hospital during the last five years than in the first five years. The frequency among the private patients fell from 1 in 12 to 1 in 16, and among the public ward patients from 1 in 29 to 1 in 33, although the total incidence in the hospital remained approximately 4.2 per cent.

Fig. 3 shows that the classical cesarean section was performed in about half the public ward cases and in about three-fifths of the private cases. The lower segment operation was somewhat more popular on the public side of the hospital, but the chief differences were in the extraperitoneal type, which was increased three times, and in cesarean hysterectomy, which was one and one-half times more frequent. These differences reflected the greater number of complicated cases admitted to the public wards.

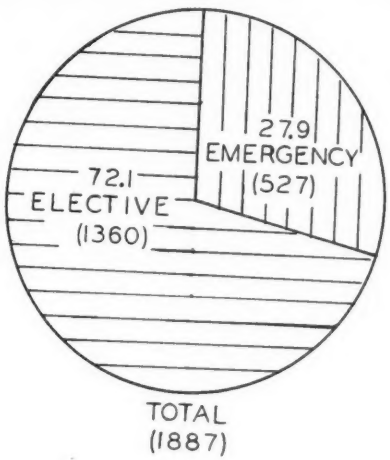

Fig. 5.

Fig. 4 demonstrates that the Kroenig (longitudinal incision) operation was performed in about three-fourths of all cases of lower segment operation, but that the preponderance was more marked on the public side than in the private wing, where two-fifths of the operations were of the transverse, or Kerr, variety.

TABLE I. RELATIVE FREQUENCY OF DIFFERENT TYPES OF EXTRAPERITONEAL CESAREAN SECTIONS

	ALL TYPES	WATERS		LATZKO		SMITH EXCLUSION		MARSUPIALIZATION	
	NO.	(NO.)	(%)	(NO.)	(%)	(NO.)	(%)	(NO.)	(%)
Public	101	40	39.6	38	37.6	14	13.9	9	8.9
Private	23	19	82.6	2	8.7	0	00.0	2	8.7
Total	124	59	47.7	40	32.1	14	11.3	11	8.9

Table I shows the relative frequency of the different types of extraperitoneal cesarean sections.

Fig. 5 indicates that about three-fourths of the operations were elective. This proportion holds for both the public and private patients.

TABLE II. FREQUENCY OF STERILIZATION

Total cesarean sections		1,887
Number sterilized		460
Per cent sterilized		24.4
Types of operations:	(No.)	(%)
Irving	414	90.0
Pomeroy	39	8.5
Salpingectomy	3*	9.7
Partial salpingectomy	2	0.4
Defundation of uterus	2	0.4
	460	100.0

*One following an unsuccessful Pomeroy in the last pregnancy.

Table II shows that approximately one-fourth of all cases (24.4 per cent), both public ward and private, were sterilized at the time of operation. Comparable figures are those of 33.7 per cent for the City of Philadelphia in 1941, and 46.5 per cent for the Chicago Lying-in Hospital. Two patients who had been subjected to the Pomeroy method of sterilization had become pregnant.

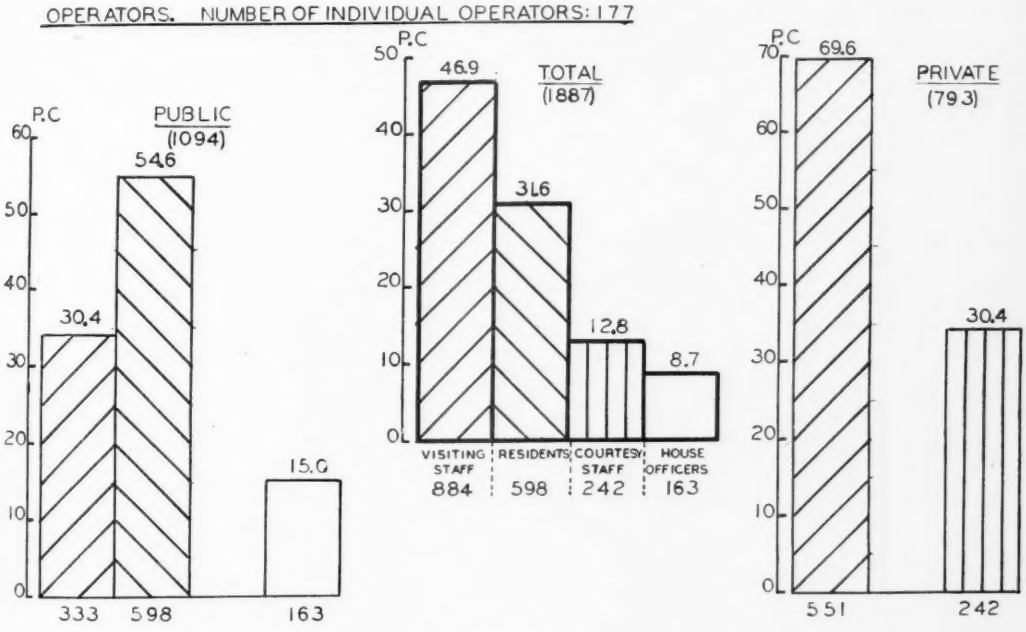

Fig. 6.

On the other hand, 413 patients, or 90 per cent of those sterilized, were operated on by Irving's method, which, in brief, consists of division of the tubes about 1½ inches from their uterine ends and their implantation into the myometrium, where they are stitched in place. No failures have resulted from this operation. Although the Pomeroy or Madlener operation is easy, it is unsuccessful often enough so that the operator may afford to spend a few more minutes performing an operation which offers the assurance of permanent sterility.

TABLE III. RELATIVE FREQUENCY OF VARIOUS TYPES OF ANESTHESIA

ANESTHETIC	PUBLIC (NO.)	PUBLIC (%)	PRIVATE (NO.)	PRIVATE (%)	TOTAL (NO.)	TOTAL (%)
N_2O-O_2-Ether	503	46.0	445	56.1	948	50.2
Spinal	71	6.5	190	24.0	261	13.8
Open ether	133	12.2	62	7.8	195	10.4
Local	145	13.2	25	3.2	170	9.0
Cyclopropane	103	9.4	38	4.8	141	7.5
Ether-O_2	62	5.7	15	1.9	77	4.1
Vinethene	62	5.7	1	0.1	63	3.3
Pentothal	14	1.2	11	1.3	25	1.3
Avertin	1	0.1	6	0.8	7	0.4
Total	1,094	100.0	793	100.0	1,887	100.0

Table III lists the anesthetics employed. Nitrous oxide, oxygen, and ether were used in half the cases in the whole hospital. Spinal anesthesia, employed in 13.8 per cent, was the next most popular, but it was given over three and one-half times more often on the private than on the public side. A practical objection to spinal anesthesia in obstetrics is the frequency of postanesthetic headaches.

Fig. 6 shows that the resident obstetricians performed over half the operations on the public ward patients, and that in the entire hospital the visiting staff performed less than half. There were 177 different operators, and the largest number of cesarean sections performed by a single operator was 162.

Indications.—The cesarean sections may be divided into those performed before viability (151) which were done mostly for medical reasons, as dystocia was not a problem, and those after viability (1,736). Fourteen (9.3 per cent) of the operations before viability were for hemorrhage. Because the medical

TABLE IV. INDICATIONS FOR CESAREAN SECTION BEFORE VIABILITY (ABDOMINAL THERAPEUTIC ABORTION). TOTAL, 151 CASES

INDICATION		NUMBER
Rheumatic heart disease (Public 42, private 4)		46
Hypertension (Public 22, private 2)		24
Hemorrhage		14
Placenta previa	5	
Premature separation placenta	6	
Rupture of uterus	1	
Threatened rupture of uterus	2	
Pre-eclampsia		11
Chronic nephritis		9
Pulmonary tuberculosis		8
Previous erythroblastotic infants		7
Pyelitis or pyelonephritis		6
Multiple sclerosis		4
Puerperal psychosis		3
Epilepsy		3
Separation symphysis pubis, progressive muscular dystrophy, and repeated fetal abnormalities: 2 each		
Rheumatoid arthritis, otosclerosis, renal tuberculosis, bilateral nephrolithiasis, surgical absence of one kidney, phlebitis, salivation, Huntington's chorea, Hodgkin's disease, and chronic invalidism: 1 each		

All these patients were sterilized except 12 (7.9 per cent) who were operated on for the following reasons: pre-eclampsia 5, premature separation of the placenta 4, and placenta previa 3.

conditions which led to these therapeutic abortions were such that future pregnancies were contraindicated, all but 7.9 per cent were also sterilized. Those not sterilized were operated on for temporary reasons, such as pre-eclampsia and hemorrhage. The preponderance of operations on the public side for rheumatic heart disease and hypertension should be noted. (Table IV.)

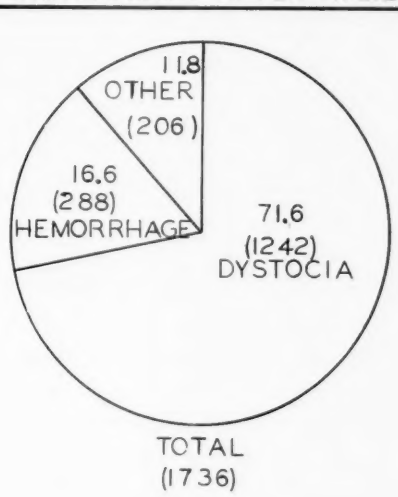

Fig. 7.

Fig. 7 shows the chief indications after viability. Seven-tenths of these operations were performed for dystocia; the rest for hemorrhage and miscellaneous reasons. These ratios compare closely for both the public and the private side.

TABLE V. DYSTOCIA AS AN INDICATION FOR CESAREAN SECTION AFTER VIABILITY (28 WEEKS); 1,242 OF 1,736 VIABLE PREGNANCIES

INDICATION	NUMBER
Previous cesarean section (Public 151, private 210)	361
Cephalopelvic disproportion (Public 181, private 75)	256
Contracted pelvis (Public 182, private 57)	239
Uterine inertia	178
Fetal distress	36
Breech	29
Gynecological repairs	27
Prolapsed cord	21
Fibroids	20
Elderly primiparity	18
Transverse	13
Previous myomectomies	7
Contraction ring	6
Previous stillbirths	6
Brow	5
Bicornuate uterus, face, and compound: 3 each	
Congenital absence cervix: 2	
Double cervix, urethral diverticulum, vaginal constriction ring, ankylosis of hip, prolapse of arm, elephantiasis, fractured pelvis, and sarcoma of sacrum and ilium: 1 each	

Table V deals with dystocia as an indication. A disproportionately large number of patients—210, or over one-fourth of the private cases—were operated on because they had had previous cesarean sections; but only 151, or about one-eighth of the public ward cases, were operated on for the same reason. It appears that a pelvic delivery after a cesarean section was a rarity on the private side. On the public side the requisites for a pelvic delivery under such circumstances are: the operation must have been done for a temporary indication such as placenta previa or a malpresentation, the convalescence must have been afebrile, the operation must have been performed by a competent surgeon, and the uterus must be explored after delivery for possible rupture. Between 1930 and 1941, 78 women with previous cesarean sections were delivered 118 times through the pelvis on the public side of the hospital without rupture of the scar occurring in a single case. Repeated cesarean sections were the chief indications for cesarean section in the entire hospital, comprising about one-fifth of all cases. Restriction of this indication would accomplish more than anything else to reduce the number of cesarean sections, particularly on the private side. Assuming that the 151 cesareans for this indication on the public side represent a reasonable figure, a comparable number for the private side would have been 109, or about half as many as were performed. As might be expected there were relatively more operations for cephalopelvic disproportion and contracted pelvis on the public side.

TABLE VI. HEMORRHAGE AS AN INDICATION FOR CESAREAN SECTION AFTER VIABILITY (28 WEEKS); 288 OF 1,736 VIABLE PREGNANCIES

INDICATION	NUMBER
Placenta previa	202
Premature separation of placenta	75
Rupture of uterus	10
Placenta accreta	1

Table VI, representing hemorrhage as an indication, suggests that the majority of the cases of placenta previa were delivered by cesarean section. On the other hand, most cases of premature separation of the placenta, particularly the type with internal hemorrhage—ablatio placentae—were delivered through the pelvis.

TABLE VII. OTHER INDICATIONS FOR CESAREAN SECTION AFTER VIABILITY (28 WEEKS); 206 of 1,736 VIABLE PREGNANCIES

INDICATION	NUMBER
Pre-eclampsia (Public 71, private 59)	130
Rheumatic heart disease (Public 28, private 7)	35
Hypertension	17
Dermoid cyst, separation of symphysis, and for sterilization: 3 each	
Eclampsia, osteitis fibrosa cystica, chronic nephritis, and no indication given: 2 each	
Pyelitis, congenital heart disease, multiple myelomas, acute appendicitis, previous sterility, previous postpartum hemorrhage, and postmaturity: 1 each	

Only 130 cesarean sections were performed for pre-eclampsia and these cases were proportionately divided between the two sides of the hospital. (Table VII.) There is a considerable preponderance of rheumatic heart disease on the public side of the hospital because many of these patients are referred by outside doctors. Only three patients were subjected to cesarean section so that they might be sterilized—all on the private side. The policy governing the public ward patients is opposed to cesarean section for this purpose, nor is it the custom of the hospital to perform sterilizations through a keyhole incision within the first twenty-four or forty-eight hours after pelvic delivery. (Table VIII.)

TABLE VIII. INDICATIONS FOR STERILIZATION WITH VIABLE PREGNANCIES (ENTIRE HOSPITAL); 321 OF 1,736 CASES (18.5 PER CENT)

	NUMBER	PER CENT
Previous cesareans	213	66.4
Gynecologic operations	29	9.4
Hypertension	25	7.8
Rheumatic heart disease	24	7.5
Excessive multiparity	17	
Fibroids	3	
Pulmonary tuberculosis	2	

Multiple sclerosis, osteitis fibrosa cystica, multiple myelomas, myesthesia gravis, chronic nephritis, surgical absence one kidney, previous postpartum hemorrhage, separation symphysis pubis: 1 each

TABLE IX. INDICATIONS FOR CESAREAN HYSTERECTOMY

INDICATION	PUBLIC	PRIVATE	TOTAL
Rupture of uterus	10	2	12
Postpartum hemorrhage	1	7	8
Intrapartum infection, actual or suspected	7	0	7
Placenta accreta	6	1	7
Fibroids	4	3	7
Sterilization	3*	2	5
Total	31	15	46

*One for a previous Pomeroy sterilization that was unsuccessful.

Table IX shows, as might be expected, that rupture of the uterus was more common on the public side. Postpartum hemorrhage following cesarean section sufficiently severe to necessitate removal of the uterus was seven times more common on the private side. This discrepancy is difficult to explain unless it be that hemorrhages were more effectively treated on the public than on the private side. On the other hand, hysterectomy for infection was more common on the public side.

Special Diagnostic or Therapeutic Measures.—X-rays were taken on two-thirds of the cases on the public side and twice as often as on the private side (Fig. 8). They were employed more often for pelvic measurements in dystocia cases on the public side, as well as for general diagnostic purposes, but less often for the detection of possible placenta previa.

Since multiple pregnancy usually appears once in 87 cases, it occurred less often than usual (1 in 122) on the public side, and more often than usual

(1 in 54) on the private side (Table X). X-rays were taken in 31.2 per cent of the cases of multiple pregnancy on the private side and 24.4 per cent on the public side. When twins or triplets are suspected, a confirmatory x-ray is practically the rule; hence it would appear that in over half the cases on both sides of the hospital, the operator may have been surprised when he delivered twins at cesarean section.

TABLE X. MULTIPLE PREGNANCY

	INFANTS (NO.)	TWINS (PAIRS) (NO.)	(RATIO)	TRIPLETS (SETS) (NO.)	(RATIO)	MULTIPLE PREGNANCY (NO.)	(RATIO)
		9	1:122	0	0:0	9	1:122
Public	1,103	15	1:54	1	1:810	17	1:48
Private	810	—		—		—	
Total	1,913	24	1:80	1	1:1,913	26	1:74

TABLE XI. TRANSFUSIONS

	NO. OF CESAREANS	PATIENTS TRANSFUSED	PER CENT
Public	1,094	95	8.7
Private	793	20	2.5
Total	1,887	115	6.1

Transfusions were performed three times more often on the public side (Table XI). In the whole hospital, patients undergoing cesarean section were transfused at the rate of one in every 16. A relatively small number of patients required uterine packing (Table XII).

TABLE XII. UTERINE TAMPONADE

	NO. OF CESAREANS	NUMBER PACKED	PER CENT
Public	1,094	19	1.7
Private	793	12	1.5
Total	1,887	31	1.6

TABLE XIII. ADDITIONAL OPERATIONS; 35 OF 1,887 CASES (1.9 PER CENT)

OPERATION	NUMBER
Myomectomy	21
Repair of incisional hernia	4
Oophorectomy	4
Appendectomy	3
Unilateral salpingo-oophorectomy, ventral suspension, and excision of adenomyoma: 1 each	

Additional operations (Table XIII) were performed in about 2 per cent of the cases. The three appendectomies were performed on private cases.

Morbidity.—In determining morbidity the so-called international standard was used: any convalescence which showed a rise in temperature of 100.4° F. or more on any two successive days after the first day and before the eleventh, was considered febrile. Fig. 9 indicates that there was no appreciable difference in morbidity between the classical and lower segment operations, that the inci-

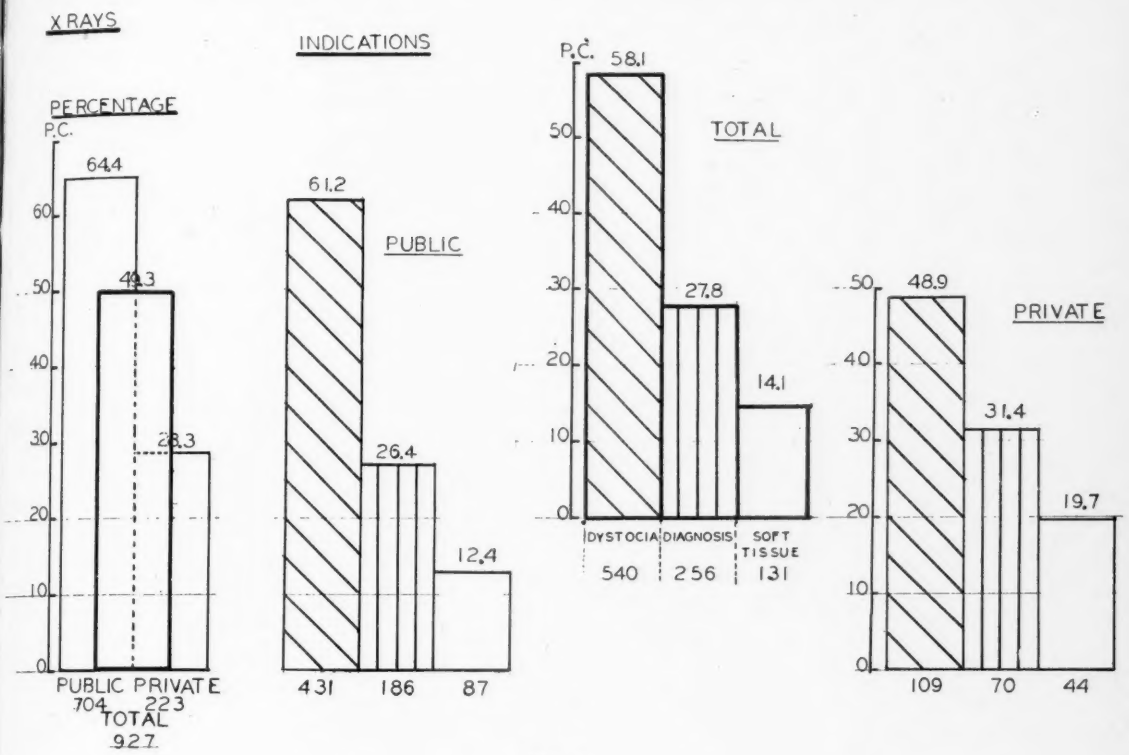
X RAYS
PERCENTAGE
P.C.
64.4
49.3
28.3
PUBLIC PRIVATE
704 223
TOTAL
927
INDICATIONS
61.2
PUBLIC
26.4
12.4
431 186 87
P.C. 58.1
TOTAL
27.8
14.1
DYSTOCIA DIAGNOSIS SOFT TISSUE
540 256 131
48.9
PRIVATE
31.4
19.7
109 70 44

Fig. 8.

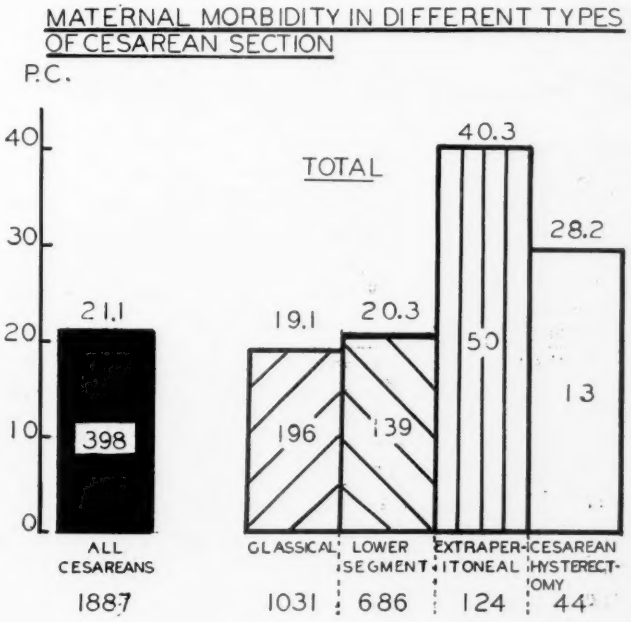
MATERNAL MORBIDITY IN DIFFERENT TYPES OF CESAREAN SECTION
P.C.
21.1
398
ALL CESAREANS
1887
TOTAL
19.1
20.3
40.3
28.2
196
139
50
13
CLASSICAL LOWER SEGMENT EXTRAPERITONEAL CESAREAN HYSTERECTOMY
1031 686 124 44

Fig. 9.

dence of morbidity was higher in cesarean hysterectomy, but that it was about twice as high in the extraperitoneal operation as in the classical and lower segment operations. Morbidity was notably lower in the private cases: 16.5 per cent in the private and 24.5 per cent in the public cases. The total morbidity was 21.1 per cent as compared with the usual hospital morbidity, which runs between 3½ and 5 per cent. The Chicago Lying-in Hospital reports a morbidity of 43.8 per cent, the Cleveland Maternity Hospital 45 per cent, the Methodist Episcopal Hospital 50.1 per cent, and the City of New Orleans[6] 61.3 per cent. The Boston Lying-In Hospital morbidity compares very favorably with all these; in fact, it is difficult to understand why they are so high. It has never been the policy at the Boston Lying-In Hospital to carry out any kind of vaginal antisepsis before cesarean section, and the relatively low morbidity following these 1,887 operations justifies this policy. Rupture of the abdominal wound following cesarean section occurred once in 629 cases and more often on the public side (Table XIV). There are no figures from other clinics available for comparison. The skin preparation for cesarean section was the same throughout the ten years. It consists of a soap and water scrub and the application of alcohol, ether, and 3½ per cent tincture of iodine. Abdominal wounds are closed in layers with chromic catgut and the skin with silk. Stay sutures are seldom used.

TABLE XIV. RUPTURE OF ABDOMINAL WOUNDS

	NO. OF CESAREANS	NO. OF RUPTURES	RATIO
Public	1,094	2	1:547
Private	793	1	1:793
Total	1,887	3	1:629

TABLE XV. FETAL MORTALITY

	PUBLIC	PRIVATE	TOTAL
Total infants born	1,103*	810†	1,913
Nonviable infants	112	42	154
Viable infants	991 (89.8%)	768 (94.8%)	1,759 (91.9%)
Stillbirths of viable infants	28	11	39
Per cent: Stillbirths	2.8	1.4	2.2
Neonatal deaths of viable infants	50	31	81
Per cent: Neonatal deaths	5.0	4.0	4.6
Stillbirths and neonatal deaths	78	42	120
Net fetal mortality	7.8%	5.5%	6.8%
Total infants dead	190	84	274
Gross fetal mortality (nonviable, stillbirths, neonatal deaths)	19.0%	10.9%	15.6%

*1,094 single births plus 9 pairs of twins.
†793 single births plus 15 pairs of twins and 1 set of triplets.

Fetal Mortality.—There is lack of uniformity in reporting fetal mortality following cesarean section. Some authors record the gross fetal mortality, which consists of nonviable infants, stillbirths, and neonatal deaths; others report only stillbirths. It seems fair to eliminate nonviable infants, inasmuch as there was no expectation of obtaining a living child in these operations, which were in effect therapeutic abortions. It seems equally fair to count stillbirths and neonatal deaths occurring after the date of viability as fetal losses.

Table XV indicates that the total net fetal mortality was 6.8 per cent, that it was 7.8 per cent among the public ward cases and 5.5 per cent among the private cases. In comparing the fetal mortality of the Boston Lying-In Hospital in cesarean section with that reported from the sources already quoted, it appears to be about average (Table XVI). Table XVII indicates that there were an unduly large number of stillbirths on the public side, due to intrauterine asphyxia.

TABLE XVI. FETAL MORTALITY IN CESAREAN SECTION AS REPORTED BY VARIOUS AUTHORS; SERIES OF APPROXIMATELY 1,000 OR MORE CASES

AUTHORS	SOURCES	CESAREANS (NO.)	FETAL MORTALITY (%)
Manahan, Connally, and Eastman[7]	John Hopkins Hospital	1,333	6.0
Daily[2]	Chicago Lying-in Hospital	1,000	6.7
Mathews and Acken[3]	Methodist-Episcopal Hospital	1,066	5.2
DeNormandie[4]	State of Massachusetts	11,030	8.2
King[6]	City of New Orleans	1,108	10.8

TABLE XVII. CAUSES OF STILLBIRTHS AND NEONATAL DEATHS

		NUMBER
Stillbirths:		39
Intrauterine asphyxia (Public 22, private 7)	29	
Erythroblastosis	5	
Hydrocephalus, intracranial hemorrhage, diaphragmatic hernia, broncho-pneumonia, and toxemia: 1 each		
Neonatal deaths:		81
Prematurity (Public 21, private 12)	33	
Atelectasis (Public 12, private 9)	21	
Intracranial hemorrhage (Public 8, private 4)	12	
Pneumonia, erythroblastosis, and congenital heart disease: 4 each		
Atresia of esophagus, multiple congenital abnormalities, and congenital intestinal obstruction: 1 each		

TABLE XVIII. FETAL MORTALITY AMONG FULL-TERM INFANTS (OVER 5 POUNDS) WITH DIFFERENT ANESTHETICS USED IN CESAREAN SECTION; TOTAL CASES

ANESTHETIC	INFANTS (NO.)	STILLBIRTHS (NO.)	STILLBIRTHS (%)	NEONATAL DEATHS (NO.)	NEONATAL DEATHS (%)	TOTAL FETAL MORTALITY (NO.)	TOTAL FETAL MORTALITY (%)
N_2O-O_2-Ether	855	22	2.6	23	2.8	45	5.4
Spinal	203	4	2.0	4	2.0	8	4.0
Open ether	172	3	1.7	2	1.2	5	2.9
Local	103	1	1.0	9	8.7	10	9.7
Cyclopropane	116	1	0.9	3	2.5	4	3.4
Ether-O_2	67	3	4.5	1	1.5	4	6.0
Vinethene	60	1	1.7	1	1.7	2	3.4
Pentothal	20	0	0.0	1	5.0	1	5.0
Avertin	7	0	0.0	0	0.0	0	0.0
Totals	1,603	35	2.2	44	2.7	79	4.9

In an attempt to determine the influence of anesthesia, if any, upon fetal mortality, two tables were prepared. The first (Table XVIII) shows the results obtained under different forms of anesthesia among full-term infants. Provided

the operation began with a living fetus in utero, anesthesia may be assumed to have had some possible effect in causing stillbirths. Its effect upon neonatal deaths is by no means so close, since other factors—notably prematurity—may come into play. Of the anesthetics most widely used, cyclopropane, local anesthesia, and open ether gave the best results so far as full-term infants were concerned.

Table XIX was prepared to determine the effect of anesthetics, if any, upon premature infants, since it is admitted that such fetuses in utero are more susceptible to drugs given to the mother than are full-term infants. Here spinal and local anesthesia gave the best results.

TABLE XIX. FETAL MORTALITY AMONG PREMATURE INFANTS (UNDER 5 POUNDS) WITH DIFFERENT ANESTHETICS USED IN CESAREAN SECTION; TOTAL CASES

ANESTHETIC	INFANTS (NO.)	STILLBIRTHS (NO.)	STILLBIRTHS (%)	NEONATAL DEATHS (NO.)	NEONATAL DEATHS (%)	TOTAL FETAL MORTALITY (NO.)	TOTAL FETAL MORTALITY (%)
N_2O-O_2-Ether	54	3	5.5	20	37.1	23	39.0
Spinal	38	1	2.6	7	18.4	8	21.0
Local	35	1	2.8	11	31.4	12	34.2
Cyclopropane	13	0	0.0	4	30.8	4	30.8
Open ether	6	0	0.0	1	16.7	1	16.7
Ether-O_2	5	0	0.0	0	00.0	0	00.0
Vinethene	2	0	0.0	1	50.0	1	50.0
Pentothal	2	0	0.0	1	50.0	1	50.0
Totals	155	5	3.2	45	29.0	50	32.2

TABLE XX. MATERNAL MORTALITY, 1934 TO 1943 INCLUSIVE

	NO. OF CESAREANS	DEATHS	PER CENT
Public	1,094	15	1.4
Private	793	9	1.1
Total	1,887	24	1.3

TABLE XXI. MATERNAL MORTALITY IN THE TWO FIVE-YEAR PERIODS BETWEEN JAN. 1, 1934, AND JAN. 1, 1944

PERIODS	NO. OF CESAREANS	DEATHS	PER CENT
First 5-year period (1934-1938 inclusive)			
Public	604	12	2.0
Private	308	5	1.6
Total	912	17	1.9
Second 5-year period (1939-1943 inclusive)			
Public	490	3	0.6
Private	485	4	0.8
Total	975	7	0.7

Maternal Mortality.—The total maternal mortality for the ten-year period (Table XX) was 1.3 per cent. It was 1.1 per cent on the private side and 1.4 per cent on the public side. When we divide the ten years into two five-year periods, we find that the total mortality in the second period is approximately

one-third of that in the first, being 0.7 per cent (Table XXI). We also see that in the last five years the mortality on the public ward was less than that on the private side, although the maternal mortality among the private patients had diminished by one-half. The death rate on the public side, however, was only one-third of its former figure. Comparing the maternal mortality rates with those quoted from the sources already mentioned, we find that the only comparable death rate is that of the Chicago Lying-in Hospital, which covers approximately half the number of cases in our ten-year series but may be compared with approximately the same number of our cases in the last five years. In the ten-year period, 1931 to 1941, the Cleveland Maternity Hospital, in 1,317 cesarean sections, also had a death rate of only 1.7 per cent (Table XXII).

TABLE XXII. MATERNAL MORTALITY IN CESAREAN SECTION AS REPORTED BY VARIOUS AUTHORS; SERIES OF APPROXIMATELY 1,000 OR MORE CASES

AUTHORS	SOURCES	CESAREANS (NO.)	MATERNAL MORTALITY (%)
Manahan, Connally, and Eastman[7]	Johns Hopkins Hospital	1,333	2.5
Daily[2]	Chicago Lying-in Hospital	1,000	0.8
Mathews and Acken[3]	Methodist-Episcopal Hospital	1,066	3.18
DeNormandie[4]	State of Massachusetts	11,030	2.46
King[6]	City of New Orleans	1,108	5.9
Lull[5]	City of Philadelphia	894	2.46
Barney, Fish, and Riemenschneider[1]	Cleveland Maternity	1,317	1.7

Fig. 10 shows the maternal mortality in various types of cesarean section. The general mortality was somewhat better with the classical operation than with the lower segment operation, and, as might be expected, there is an increased mortality with the extraperitoneal operation and with cesarean hysterectomy. It is noteworthy that 278 lower segment operations were performed on the private side with only one death, a mortality rate of 0.4 per cent. Morbidity and mortality was considerably lower in the elective than in the emergency operations (Table XXIII).

TABLE XXIII. MORBIDITY AND MATERNAL MORTALITY IN ELECTIVE AND EMERGENCY CESAREAN SECTIONS

	TOTAL	FEBRILE (NO.)	FEBRILE (%)	DIED (NO.)	DIED (%)
Elective	1,360	252	18.5	14	1.0
Emergency	527	146	28.8	10	1.9

TABLE XXIV. MATERNAL MORTALITY IN DIFFERENT TYPES OF LOWER SEGMENT CESAREAN SECTION

	KROENIG (LONGITUDINAL INCISION) (NO.)	(DEATHS)	(%)	KERR (TRANSVERSE INCISION) (NO.)	(DEATHS)	(%)
Public	337	3	0.9	71	2	2.8
Private	166	1	0.6	112	0	0.0
Total	503	4	0.8	183	2	1.1

Table XXIV indicates that in the entire hospital a somewhat lower mortality was obtained with the Kroenig (longitudinal incision) operation than with the Kerr (transverse incision), although better results with the Kerr operation were obtained on the private than on the public side.

TABLE XXV. MATERNAL MORTALITY IN DIFFERENT TYPES OF EXTRAPERITONEAL CESAREAN SECTION

	WATERS			LATZKO			SMITH EXCLUSION			MARSUPIALIZATION		
	(NO.)	(DEATHS)	(%)	(NO.)	(DEATHS)	(%)	(NO.)	(DEATHS)	(%)	(NO.)	(DEATHS)	(%)
Public	40	2	5.0	38	1	2.6	14	0	0.0	9	0	0.0
Private	19	0	0.0	2	0	0.0	0	0	0.0	2	0	0.0
Total	59	2	3.4	40	1	2.5	14	0	0.0	11	0	0.0

Table XXV indicates that of the different types of extraperitoneal cesarean section the lowest mortality followed the Smith exclusion and the marsupialization operations. It should be realized, however, that these operations, particularly the Smith exclusion, were employed in cases where infection was not always definitely established.

TABLE XXVI. CAUSES OF DEATH

CAUSES OF DEATH	PUBLIC	PRIVATE	TOTAL
Peritonitis	7	3	10
Hemorrhage	2	5	7
Pulmonary embolism	2	1	3
Eclampsia	1	0	1
Intestinal obstruction	1	0	1
Bronchopneumonia	1	0	1
Malignant endocarditis	1	0	1
Total	15	9	24

Table XXXVI, listing the causes of death, indicates a preponderance of fatalities from peritonitis on the public side and from hemorrhage on the private side. There was only one death in the 1,887 cases which was attributed to anesthesia. This patient took her anesthetic badly, regurgitated vomitus, and died on the second postoperative day of bronchopneumonia. Of the ten cases that died from peritonitis, five had been in labor for periods of five, seventeen, seventeen, twenty, and twenty-six hours, respectively; the membranes had been ruptured in three cases for three, thirty, and ninety-six hours, respectively; and a fever was present in four cases. Two patients had respiratory infections; one of these women was operated on under local, and one under spinal anesthesia, but while pneumonia did not develop in either case, peritonitis did. One of these two patients was in labor and the operation was of an emergency nature; the other, however, was not in labor and the operation could have been postponed. These factors would indicate, since six of the operations were of the classical and four of the lower segment type, that greater safety might have been secured for these patients had the extraperitoneal approach been used, particularly since none of the three deaths following the 124 extraperitoneal cesarean sections resulted from infection. If the uterine contents is infected at

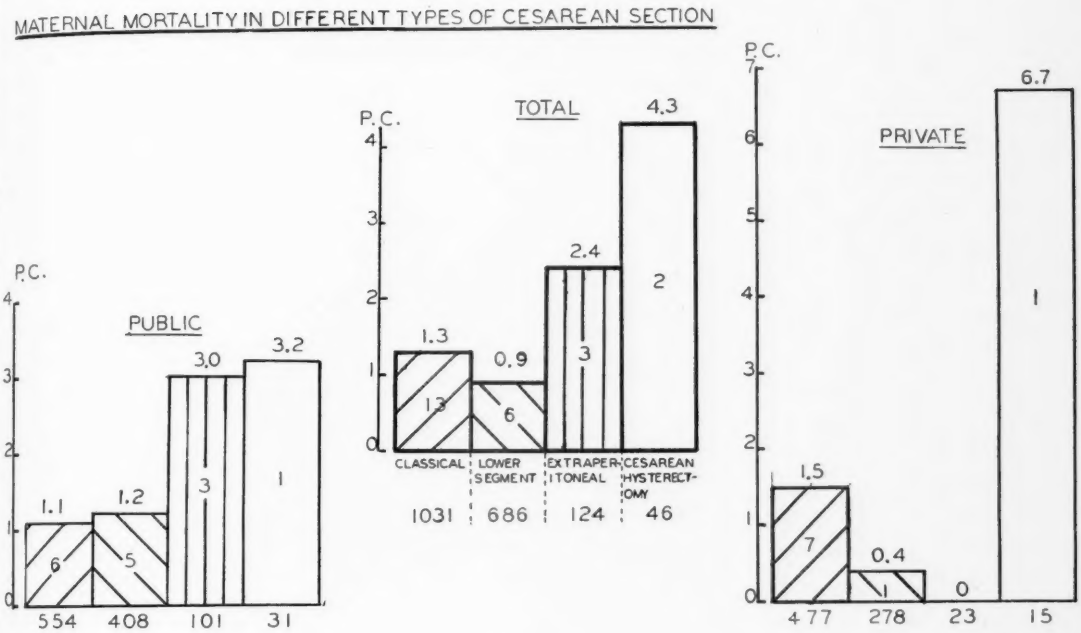
MATERNAL MORTALITY IN DIFFERENT TYPES OF CESAREAN SECTION
P.C.
PUBLIC
1.1
1.2
3.0
3.2
6
5
3
1
554
408
101
31
TOTAL
4.3
2.4
1.3
0.9
2
3
13
6
CLASSICAL
LOWER SEGMENT
EXTRAPERITONEAL
CESAREAN HYSTERECTOMY
1031
686
124
46
PRIVATE
6.7
1.5
0.4
0
7
1
477
278
23
15

Fig. 10.

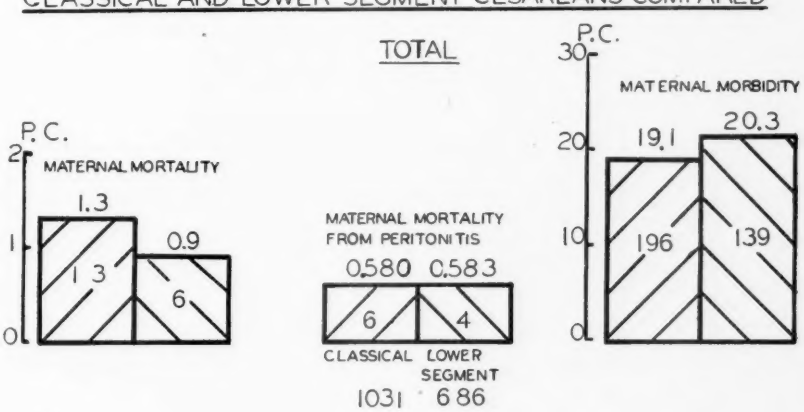
CLASSICAL AND LOWER SEGMENT CESAREANS COMPARED
P.C.
MATERNAL MORTALITY
1.3
0.9
1 3
6
TOTAL
MATERNAL MORTALITY FROM PERITONITIS
0.580
0.583
6
4
CLASSICAL
LOWER SEGMENT
1031
686
P.C.
MATERNAL MORBIDITY
19.1
20.3
196
139

Fig. 11.

the time of operation we believe that the lower segment operation gives no greater security against peritonitis than does the classical.

Fig. 11 indicates that there was little difference in general maternal mortality, mortality due to peritonitis, and morbidity between the lower segment and the classical operation.

TABLE XXVII. MATERNAL MORTALITY ACCORDING TO STAFF POSITION OF OPERATORS

OPERATORS	NO. OF CESAREANS	NO. OF DEATHS	PER CENT
Visiting staff	884	12	1.4
Residents	598	7	1.2
Courtesy staff	242	4	1.6
House officers	163	1	0.6
Total	1,887	24	1.3

A glance at Table XXVII would suggest that the best way to secure a low death rate in cesarean section would be to delegate all the operating to the least experienced persons on the staff—the house officers, or interns. It should be obvious, however, that cases for operation, aside from the private patients, were assigned according to their seriousness. Moreover, the fact that 1,887 operations were performed by 177 operators with uniformly good results should indicate that why, when, and how the operation is done is quite as important as who does it.

The advocates of spinal anesthesia list as one of its advantages the alleged fact that the uterus contracts well at cesarean section. Table XXVIII, however, shows that it contracted so badly in three of 261 cases that it was necessary to remove it. Indeed, unless one accepts the relatively high incidence of hysterectomy for hemorrhage with ether-oxygen anesthesia in a small series of 77 cases, it does not appear that any anesthetic had a predominant effect toward producing postpartum hemorrhage in this series.

TABLE XXVIII. ANESTHESIA AND HYSTERECTOMY FOR HEMORRHAGE AT CESAREAN SECTION

ANESTHETIC	NO. OF CESAREANS	NO. OF HYSTERECTOMIES	PER CENT
N_2O-O_2-Ether	948	3	0.31
Spinal	261	3	1.14
Ether-oxygen	77	2	2.59

Cesarean Section as a Method of Delivery in Certain Complications of Pregnancy and Labor Other Than Dystocia.—Tables XXIX, XXX, and XXXI are designed to show the advantages or disadvantages of cesarean section compared with pelvic delivery in three of the common complications of pregnancy. These data are taken entirely from the public service. Table XXIX shows that cesarean section was the favorite method of treating placenta previa as it was employed in almost two-thirds of the cases. Among the patients so delivered, 113, there was only one death, a mortality rate of 0.9 per cent. The death rate was three times lower than the rate among those delivered through the pelvis; moreover, the fetal mortality was only one-fourth as high. In fairness, however,

TABLE XXIX. CESAREAN SECTION IN THE TREATMENT OF PLACENTA PREVIA. 181 PUBLIC WARD CASES. 1934 TO 1943

DELIVERED BY	NO. OF CASES	% OF TOTAL	MATERNAL DEATHS	MATERNAL MORTALITY %	STILLBIRTHS AND NEONATAL DEATHS	FETAL MORTALITY (%)
Cesarean	113	62.5	1	0.9	17	15.2
Other methods	68	37.5	2	2.9	41	60.4
Totals	181	100.0	3	1.6	58	32.0

TABLE XXX. CESAREAN SECTION IN THE TREATMENT OF PREMATURE SEPARATION OF THE PLACENTA; 368 PUBLIC WARD CASES, 1934 TO 1943

DELIVERED BY	NO. OF CASES	% OF TOTAL	MATERNAL DEATHS	MATERNAL MORTALITY %	STILLBIRTHS AND NEONATAL DEATHS	FETAL MORTALITY (%)
Cesarean	45	14.2	1	2.4	8	17.8
Other methods	323	85.8	7	2.2	140	43.3
Totals	368	100.0	8	2.2	148	40.3

TABLE XXXI. CESAREAN SECTION AS A METHOD OF DELIVERY IN PRE-ECLAMPSIA; 2,877 PUBLIC WARD CASES, 1934 TO 1943

DELIVERED BY	NO. OF CASES	% OF TOTAL	MATERNAL DEATHS	MATERNAL MORTALITY %	STILLBIRTHS AND NEONATAL DEATHS	FETAL MORTALITY (%)
Cesarean	76	2.7	1	1.3	12	15.7
Other methods	2,801	97.3	9	0.3	238	8.5
Totals	2,877	100.0	10	0.3	250	8.7

it must be stated that cases where the fetus was dead, nonviable, or grossly malformed were usually selected for pelvic delivery. Probably the indications for cesarean section in placenta previa can be extended. On the other hand, cesarean section was not the method of choice for delivering patients with premature separation of the placenta, as only slightly over one-eighth were delivered that way (Table XXX). It should be understood that all cases of premature separation of whatever degree of seriousness are included in this total, and that almost all cases of ablatio placentae were delivered through the pelvis as is suggested by the high fetal mortality (43.3 per cent). Cesarean section in premature separation was reserved for cases where the baby was alive, the degree of blood loss slight to moderate, and shock absent. The only exceptions were made when conservative measures—rupture of the membranes and the application of a pressure abdominal binder—were ineffective in bringing about delivery. There appears to be no reason to change this policy. It is evident from Table XXXI that conservative measures, either spontaneous or artificial, for evacuation of the uterus in pre-eclampsia was the rule, as only 2.7 per cent were delivered by cesarean section. This operation was reserved for cases where delivery was urgently indicated and the cervix, being long and rigid, was unfavorable for induction. The results confirm the wisdom of this policy. Pelvic delivery was accompanied by a maternal mortality of one-fourth and by a fetal death rate of about one-half of that in cesarean section.

We are now in a position to answer the questions raised in the first part of this paper: (1) Judging by the frequency of cesarean section in other institutions, the incidence among the public ward patients at the Boston Lying-In Hospital does not appear excessive. The relative frequency among the private patients on the other hand, being over twice that of the public ward, is the highest reported from any clinic, the only comparable figure being that from the Cleveland Maternity—6.3 per cent among its service cases. (2) The chief causes of maternal death on the public side was peritonitis and on the private side hemorrhage. Peritonitis might have been avoided by more frequent resort to extraperitoneal cesarean in questionable cases, and deaths from hemorrhage by more prompt transfusion. During the past year a hospital blood bank has been established where an adequate supply of group O, Rh-negative blood is always on hand. This precaution should do much to diminish the number of deaths from hemorrhage. The chief cause of stillbirth was intrauterine asphyxia, and the chief causes of neonatal death were prematurity, atelectasis, and intracranial hemorrhage. It should be remembered that a number of deliveries by cesarean section, particularly on the public side, were indicated in the interests of the mother, rather than those of the babies, and that in such cases a fairly high fetal death rate must be expected. In some cases, however, tests of labor, which were finally terminated by cesarean section, were extended to such a point that the fetuses suffered in utero and were either born dead or died in the early days of life. The twelve cases of intracranial hemorrhage belong to this group. (3) For the ten-year period the maternal mortality is somewhat lower on the private side, but for the last five years the maternal mortality is somewhat lower on the public side. Fetal mortality is distinctly lower on the private side and this is probably due to the fact that few, if any, long tests of labor were conducted, and fewer cesarean sections were performed there primarily for the sake of the mother. (4) Maternal mortality compares favorably with that reported from other clinics. The fetal mortality is about average.

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A REVIEW OF THE PROBLEM OF CANCER OF THE CERVIX SINCE THE USE OF RADIUM IN 1912

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AT THE time this narrative begins, progress in the treatment of cancer of the cervix had been attempted mainly by improving the technique of the so-called advanced radical operation. This plan of operation had been preceded first by simple vaginal hysterectomy and then by high amputation of the cervix (Byrne) or vaginal hysterectomy (Werder) with the cautery.

W. A. Freund had followed by advising, in 1878, operation by the abdominal route, and a more radical procedure with dissection of the ureters had been suggested by Ries in 1895 and put into practice by Clark and Rumpf in 1896, the burden of the operator being the more extensive removal en bloc of the parts in contact with the carcinomatous cervix—the upper vagina, the parametrium, and the enlarged iliac and obturator pelvic glands.

The leaders in this and foreign countries vied with each other in the percentage of operability, mortality, and five-year results. It remained for Wertheim to publish first (1911) the operative results in a large series of patients (500); in half of them the operation had been performed more than five years previously. His percentage of operability was 50. His initial mortality was very high: 30 per cent of the first hundred, but reduced to 15 per cent in the last hundred and not at the expense of excluding the more advanced cases; 57.6 per cent of those surviving the operation and 42.9 per cent of all operative patients were alive and cancer-free at the end of five years; this meant an absolute survival rate of 18.4 per cent. The excellence of his work led to the adoption of the term "Wertheim operation" for the radical procedure.

In the days of which we have been speaking, when cancer affected the tissues to such an extent that no radical removal could be attempted, the carcinomatous areas were curetted and cauterized and the unfortunate victim was left to applications of acetone or formalin or to deodorizing douches for the foul discharge, and opiates for the pain.

The adoption of radium in 1912 as a treatment of choice by Kelly and Burnham, who by that time had approximately a gram of radium, marked the beginning of an epoch; the visual results of treating extensive cancers of the cervix were so startling as to seem miraculous. Here at last was an agent which had the power of destroying cancer cells.*

The gamma rays from a radium salt or a radium emanation and the gamma rays of the x-ray have loomed large as factors in the treatment of cancer ever since and, to a very considerable extent, have taken the place of radical surgery.

*Louis Wickham and his colleagues, particularly Cheron, should be credited with a limited number of cases prior to 1912; Kelly started in 1908 with a small amount of radium.

In the inevitable comparison between irradiation and operation there has been a constant effort by many writers to make a trustworthy estimate of the real worth of both forms of treatment. Many difficulties lie in the way, as will be shown, and in more recent years a combination of irradiation and operation have appeared to complicate the picture.

Extent of the Disease

To begin with, the extent of the lesion at the start of observation and treatment is of much importance. Schmitz first proposed (1927) a classification into four groups and this was modified later by others, among them the League of Nations Health Organization.

Cancer statistics have shown that the earlier the lesion is found the more effectual were all forms of treatment, and many efforts have been made to get hold of the cancer patient with the least delay. As early as 1905 the Section on Obstetrics, Gynecology and Abdominal Surgery of the American Medical Association had formulated a letter to be sent to every member of every County Medical Society emphasizing the early symptoms and recommending instruction of the lay woman.

Much good has been accomplished by the American Society for the Control of Cancer, now the American Cancer Society, which has publicized among women the early symptoms. This spread of information and the cancer clinics inaugurated by Catherine Macfarlane (1938) are bringing many patients, otherwise neglected, under a physician's care.

Physicians themselves have been warned against overlooking early symptoms and the Obstetrical Society of Philadelphia with the cooperation of the County Medical Society and the Department of Public Health has recently appointed a committee for the study of pelvic cancer. Every death from pelvic cancer in Philadelphia will be investigated and a special study made of that period of the patient's history between the onset of symptoms and the institution of adequate therapy—the so-called "delay period" and the responsibility for it assigned to the patient, the doctor, or the hospital, as the case may be. It may be noted here that the "delay period" nowadays is often due to a trial of hormone treatment before proceeding to a thorough diagnostic examination. The promiscuous use of hormones in women approaching the menopause is a real danger much to be regretted.

Diagnosis of Cancer

Biopsy of the cervix or diagnostic curettage with histologic examination remains the trustworthy diagnostic criterion; the color test of Schiller (failure of Lugol's solution to stain), the colposcope of Hinselman (magnified view of the vaginal and cervical mucosa), and the vaginal smear (cancer cell differentiation from benign epithelium) method of Papanicolaou and Traut, the last the more effective of the three, direct our attention to suspected patients.

Cullen's admirable book, *Cancer of the Uterus* (1900), was of the greatest help to the worker in the laboratory, and the magnificent histologic pictures by

Brödel and Becker, drawn cell for cell from beautifully cut and stained sections, gave an impetus to the differential histologic diagnosis. Notable also were the efforts in this direction of such men abroad as Ludwig Pick and Robert Meyer who instructed aspiring gynecologic pathologists from all over the world.

Technique of Irradiation

The individual patient must be very thoroughly studied as to the exact position and extent of the carcinomatous involvement; the irradiation must be effected just where it is needed with ample protection of the surrounding areas. For this purpose the screening of the radiant substances is of the greatest importance, and various forms of containers and screens have been devised.

The acme of radium applications is achieved only when a sufficient supply of radium salt or its emanation suitably screened is at hand at the moment of application. At the start of irradiation therapy the importance of screening was not appreciated everywhere and the necessary amount of radium or its emanation was to be found in a very limited number of hospitals.

As time went on, the situation improved, and this is very important because it frequently happens that the radiologist cannot be sure of what he will need until the parts are examined under anesthesia. The dose given will depend on the screening, the extent of the lesions, and the proximity of near-by structures that must be protected.

The dose for a cervical cancer is 3,600 mg. hr. and upwards, with 1.5 mm. of platinum screening; as much as 4,000 or 5,000 mg. hr. has been given. A "massive dose" at the first treatment has been the trend for a long while, since the cancer cells are supposed to be more vulnerable then than later when sclerosis and contraction of the surrounding tissues has taken place. Nevertheless some authorities (Heyman) believe in the smaller and repeated (fractional) applications and report excellent results.

The harmful rays, alpha and beta, are entirely excluded when the radium salt is enclosed in platinum capsules of 50 mg. contents with walls 1.5 mm. thick. An equivalent filter is 2.8 mm. of lead. For 10 mg. needles of the radium salt, a 0.5 mm. platinum wall is used which takes care of 99.9 per cent of the harmful rays and solid gold walls of 0.03 mm. thickness shuts out 97.6 per cent of the objectionable rays from emanation seeds.

The treatment of cancer of the cervix by x-ray began in Germany about 1911; it reached its greatest early development at the Erlangen Clinic under the direction of Seitz and Wentz. Deep x-ray therapy has acquired a position as a desirable preliminary or adjunct to nearly every application of radium. A question to settle is whether it should come before or after the application of radium. Theoretically no doubt it should be first, since the manipulation incident to a radium application might displace cancer cells and these may spell disaster unless they have been previously exposed to the deep x-ray.

We will not discuss at length the technique of the x-ray therapy used for cancer of the cervix since that lies without the province of the gynecologic radiologist. We content ourselves with saying that while x-ray machines of 200, 400, 800 kw. and over have been used, the standard treatment at the Jeffer-

son Hospital is given by a 200 kw. machine with suitable screening through four portals of entry both anteriorly and posteriorly, and an average exposure measured by erythema of 1,600 to 2,400 r. to each area. A transvaginal port exposure of the same dose has been added since 1944.

The histologic diagnosis must be settled before any form of irradiation is started; in the average patient with suspected cervical cancer this may be determined satisfactorily by a careful biopsy with a minimum disturbance of the parts, using a sharp knife or a scissors, and sealing the area with a cautery immediately thereafter; any more than the gentlest palpation of the uterus and surrounding parts should be avoided.

Among the radiologists we may presume that the work of Heyman has not been surpassed. One reason is that when he comes to make an application of radium, everything that may be required is at his disposal. In his clinic at Stockholm of a morning there are from 500 to 800 mg. of radium at hand and more available if needed, with every conceivable size and shape of platinum capsules, needles, and filters. Another reason is the government help in Sweden whereby all patients may be kept track of, the Government paying for their transportation to and from the Radium Hemmet, so that Heyman's statistics, reflecting his diligence and care, are extraordinary in the follow-up.

To be specific, he has not lost sight of a single one in a total of 2,387 patients, and he has reported upon them in extenso as to survival, deaths, and disappearances at least up to the beginning of World War II (1939) when his total of ten-year patients had reached 1,438.

Bonney has succeeded Wertheim as the outstanding exponent of radical surgery. It is interesting to note that Wertheim in 1911 had an absolute five-year salvage in 250 patients of 18.1 per cent, and that Bonney in 1941 reported his absolute five-year salvage in 500 operations as 25 or 26 per cent;* so much for improvement!

Technique of Operation

The advanced radical hysterectomy for cancer of the cervix is a formidable operation and few gynecologists learn to carry it out expertly. Those who undertake it must be skillful naturally, they must have abundant clinical material for their apprenticeship, they must be convinced that the high mortality and morbidity which almost inevitably will attend their first cases is justified by the better results that may be achieved and so go on with a preferment of the operation despite the immediate risk.

Apropos of this we may quote Shaw, a skillful and successful surgeon, who gave up the operation despite an experience comparing well with Bonney's, amounting to 154 five-year patients, in favor of irradiation; he speaks of "fearsome" operations, "the technical difficulties of which no description ever mentions"; and also Bonney who points out that "the safety and the outcome of the operation depends upon the judgment and skill of the surgeon which increases with his experience."

*Bonney gives two figures in all his reckonings; the first includes every patient; the second excludes the patients dead from other diseases or lost.

Not all operations labeled Wertheim are really so. There is no operation in the gynecologic field that requires more care in the selection and preparation of patients, better anesthesia, and more of the utmost in technique, judgment, and postoperative treatment.

So far as the further practice and development of the radical operation is concerned, it is doubtful whether other surgeons will go as far as the pioneers, Mackenrodt and Wertheim, especially, in Germany, and Berkeley and Bonney in England. We must remember that when they began their operative experience a surgical procedure was the only available means of curing a patient of cancer. They felt justified in taking any risk no matter how great because otherwise every patient was doomed to death.

After irradiation had appeared, the picture changed, for here was a remedy which, in a certain proportion of cases, gave as good results with almost no primary mortality and with a minimum of morbidity such as ureteral fistula and the distressing symptoms sometimes following an injury to the bladder or the rectum. It is all very well to say that the results of surgery will be greatly improved because of the modern methods of combating infection and of sustaining the operative patient, but the morbidity to a certain extent from injury will still remain. It will give many a surgeon pause to subject a patient to a formidable surgical procedure when he realizes that it may prove to be no better than irradiation.

Wertheim began his work in 1898; Bonney started in 1907; it was not until 1911 or 1912 that Kelly and Burnham had enough radium to start their work in earnest and the reports of the results of irradiation (five-year salvage) did not begin to appear until 1921 or 1922; by that time Bonney had had fifteen years of operative experience; he must have been satisfied with his work for he continued with it, turning over to the radiologist only the inoperable patients.

Results of Irradiation and Operation Combined

Whether a combination of surgery and irradiation as practiced by Lynch and Taussig, master surgeons, both unfortunately deceased, will accomplish more than the radium of a Heyman or the scalpel of a Bonney is a question for the future.

Lynch declared "that surgery should be reserved for the treatment only of patients whose cancers are limited definitely to the cervix and who themselves are first-class surgical risks by reason of age and general physical condition."

He used irradiation and an advanced radical operation in a selected group of patients and compares it with irradiation alone. He published charts illustrating the results at five and at ten years which favored definitely a combination of irradiation and operation.

In the five-year estimate the salvage rate of the combined procedures was 61.5 per cent; of irradiation, 53.1 per cent; in the ten-year estimate the salvage rate of the combination was 62.9 per cent; and of the irradiation, 36.7 per cent.

These are high degrees of accomplishment. The absence of recurrence in the irradiation plus operation group between the fifth and the tenth years shown

by Lynch in his charts may be very significant; Heyman and Bonney both had an increase in recurrence during the second five years of about 10 per cent; Lynch had approximately the same difference in the patients with irradiation alone, from 53.1 per cent at five years to 36.7 per cent at ten years, but in the irradiation plus operation group the rate of salvage is set down astonishingly as 61.5 per cent at the end of the first and 62.9 per cent at the end of the second five years.

Unfortunately we find no statement in his 1940 report as to the total number of patients or the other data that permits an appraisement of the absolute results.

Similarly Taussig in his 1943 report tells us that his lymphadenectomy patients were in Group II, younger and good operative risks from the standpoint of obesity and general condition. At that time he had had 175 patients of irradiation combined with lymphadenectomy and compared them to 118 patients for whom he had used irradiation alone; the five-year survival in the first group was 38.6 per cent; in the second 26.8 per cent. Taussig's data also are not given in such detail as to permit an estimate of his absolute percentage of results.

Removal of Carcinomatous Glands

Bonney in the last edition of his textbook reported the removal of glands that were malignant in 171 of his 415 operation patients between 1907 and 1931; 28 of them survived for ten years, 16 per cent, or, if those dying from intercurrent disease or lost are excluded, 18 per cent.

Taussig's removal of enlarged lymph glands was done in combination with irradiation because he doubted the curative effect of irradiation upon them; he did not remove the cervix or the surrounding tissue. In 175 patients subjected to the combined procedure, the glands were carcinomatous in 26.8 per cent; 21 per cent of the latter survived at the five-year salvage.

The ideas of Lynch and Taussig have been followed by D. G. Morton of the University of California. He selected for lymphadenectomy as Lynch did for hysterectomy only those patients in whom the local reaction to irradiation had been favorable. In a considerable experience with 65 patients, he found the glands carcinomatous in 15 but cancer-free in 28; the involvement of glands was four times more frequent in patients who had had no preoperative x-ray.

He raises a question that occurs to us also of whether it will be shown that modern x-radiation actually may destroy cancer in lymph nodes; if so there would be some doubt as to the need of lymphadenectomy.

We may contrast the reports of Heyman the radiologist and Bonney the surgeon as a matter of general interest. Heyman had a total of 1,438 ten-year patients and Bonney 451. Heyman's patients are definitely classified; Bonney does not classify his patients and the only way we have of judging them is by his operability rate (63) for the entire series, his operability rate in private patients (80) and the number of operations (171) in which he removed carcinomatous glands. We may infer from these facts that he had many early (Groups I and II) patients but also many late (Group III) ones, but we can go no further.

Heyman reports a ten-year salvage as follows: 44 per cent in Group I; 27 per cent in Group II; 11.7 per cent in Group III and 3.3 per cent in Group IV. His absolute rate of recovery for the entire series is 17.

Bonney reports an absolute ten-year salvage of 20 or 21 per cent of all cases and a relative salvage of 16 or 18 per cent in those (171) patients from whom he removed carcinomatous glands.

Practically all patients with carcinoma of the cervix may be treated with irradiation whereas operative treatment may be selected only for those in whom the disease has not advanced beyond certain limits; this at once has a large bearing on what are spoken of as absolute and relative results. The number in the entire group of consecutive patients coming under observation and treatment during a certain time, that are entirely free of signs or symptoms of the disease at the end of a standard period of years, constitutes the absolute percentage; the number in selected groups constitutes the relative percentage.

Another very important figure is the percentage of the total number of patients who are kept under observation up to the time of the report. Wertheim, in his paper of 1911, had not lost sight of a single patient. In our own clinic, when Scheffey came to make the first five-year estimate, the whereabouts of 30 to 40 per cent of the patients were unknown. By persistent efforts he was able to search out most of them, raising the follow-up to 94 per cent at the time of publication; since then, 98.6 per cent of our patients have been kept under observation. When patients are reported lost sight of or dead from other intercurrent diseases, an element of inaccuracy is injected into the summation of results. We may venture the opinion that at least two-thirds of them have died of cancer.

Although, at first, patients with no gross or symptomatic evidence of the disease at the end of five years were regarded as cured, it was soon observed that recurrences appeared later so that the term used was changed from "cured" to "salvaged." It has been shown finally that there are many recurrences between the fifth and the tenth year but rarely later, and whereas Heyman could report 22 per cent absolute salvage of all cases at the end of five years, the figure dropped to 17 per cent at the end of ten years; and Bonney's absolute salvage, 25 or 26 per cent at five years, fell to 20 or 21 per cent at ten years.

Some of the Fallacies of Cancer Statistics

The vagaries of cancer statistics have already been pointed out in the course of this paper. It is difficult to evaluate and to compare the results of treatment, whatever it has been, in different hands. The reports are not made uniformly and one must hesitate to draw conclusions of his own relative to the total number of patients, the classes to which they belonged, the five- and the ten-year salvage in absolute and in relative terms.

To obtain uniformity in records and in reports, "perhaps a goal we still shall gain," is most desirable, but the probabilities are against it. If such a thing began at once, a period of eleven years would have to elapse before ten-year salvage could be estimated. The comprehensive, exact, and discriminating reports of

George Gray Ward of the Woman's Hospital in New York took a lead early in the study of irradiation in this country and have steadily maintained it.

The difficulties attendant upon an estimate of the class to which a cancer patient belongs at the start have been mentioned, and the difficulties in determining from a personal examination or a written or verbal report at the end of ten years, which has become the standard salvage period, are quite obvious.

Another misinterpretation threatens when reirradiation is encountered. In Scheffey's report of 1943, 36 per cent of 285 five-year patients had been reirradiated; the result in them is hardly of the same import as in those who needed only one treatment; they really represent recurrences and should be dropped, perhaps, and their salvage period started all over again. The custom at present is to keep them in their original five- and ten-year units no matter when the recurrences.

The technique of all engaged in the treatment of cancer of the cervix may change from time to time, and up-to-date statistics for new procedures require six to eleven years.

In estimating results by combining reports from various sources, there is some fallacy because radiologic treatment and operative treatment are by no means of equal merit in different hands.

A bird's-eye view may lead to the conclusion that cancer statistics merely show "which way the wind is" and are capable of misinterpretation.

We take this occasion to acknowledge the work of such men as Healey, Keene, Crossen, Novak, Norman Miller, Behney, Te Linde, and Kamperman, who have not been spoken of previously, and others for the moment forgotten. Our criticisms have been with the best intention and a full realization of the trials of the investigator.

Prospects for the Future

There are numerous reasons to believe that irradiation may be applied better as time goes on and the radiotherapeutist is supplied with an adequate amount of the salt or the emanation, perhaps in a form that will be more effectual no matter what the mechanical difficulties presented by the location of the cancer and the associated lesions in the particular case. A combination of irradiation with operation may be devised that will be more effective than either alone (Lynch, Taussig, Morton, Meigs).

It may be pertinent here to call attention to Bonney's results when every patient in his series is taken into account. As noted previously, he operated upon 63 in every hundred; 7 were beyond any form of treatment; 30 were irradiated and 1 in 5 or 6 recovered. On this basis he reaches an absolute five-year salvage of 30 or 31 per cent and a ten-year salvage of 24 or 25 per cent.

One cannot help believe that the riddle will be solved some time, with irradiation playing a large part, but maybe from some entirely new therapeutic means as yet unknown. In the last decade we have had reason to feel more hopeful of medical wonders to come. Gynecologists for years had looked for an intravenous treatment of septic infection; mercurochrome was the nearest approach to a medicine that might kill the infection and spare the patient, but

with that drug as with the others preceding it we had to acknowledge failure; yet finally the sulfonamides and the antibiotics (penicillin and streptomycin) were discovered, and a new and very advanced era began in the treatment of all forms of bacillary disease. Perhaps something revolutionary, a catalyst, that will specifically destroy cancer cells may be discovered.

In summing up, one may conclude that:

1. A greater number of cancer patients are presenting themselves in the early stage as a result of information given to the lay woman and to physicians in general; the proportion is almost bound to increase.

2. Irradiation with radium or its emanations, or by the deep x-ray, will become more widely and adequately available, better understood, and more effectual.

3. The risk attending operative procedure has been much reduced and improvement is likely to continue. Of the 93 patients lost by Wertheim in his first 500 operations, the cause of death in 39 was put down as peritonitis. With the sulfonamides, penicillin, and streptomycin, with the use of glucose, plasma, and blood transfusion, with Wangenstcen's drainage, with continuous spinal anesthesia, with prostigmine—a large proportion would have been prevented.

Meigs recently reports 47 cases of his Wertheim operation with preparatory radiation in 40 per cent and no immediate mortality; Lynch's (1940) figure was 73 radical operations with 4 deaths; Taussig (1936) 46 patients with 2 deaths. Bonney between 1907 and 1936 had performed his operation on 500 patients with 70 operative deaths, 14 per cent; in the last two hundred operations of the series the mortality had shrunken to 11 per cent. He points out the influence of the extent of the operation, as well as the age and general condition of the patient, on the primary mortality. Berkeley found in a collected series of operations by British gynecologists a mortality in advanced cases of 23.1 per cent; of early ones 6.3 per cent. Bonney estimates the risk in favorable cases as 5 and in unfavorable as 20.

4. Perhaps a combination of irradiation and operation will give better results.

During the period of time covered by this report there have been other means proposed that were believed to have a specific effect upon the cancer cell. The first of these was the theory of Beard (1905) that pancreatic ferments were curative. The second that of Blair Bell (1926) according to which lead would kill the cancer cell. Both of these plans have failed to meet the hopes held out for them and have been abandoned.

Percy's plan (1914) of cooking the carcinomatous areas by means of specially devised specula met with some early success but was lost in the advancing tide of irradiation.

We may quote with interest from an article that appeared recently in the *Statistical Bulletin* of the Metropolitan Life Insurance Company:

Among white females insured in the Metropolitan Life Insurance Company's Industrial Department, essentially an urban group, the standardized death rate from cancer at ages 1 to 74 declined steadily from 90.4 per 100,000 in 1934 to 80.3 in 1944, a decrease of 11 per cent.

There is confirmation from other sources as well that the organized movement to control cancer is bearing fruit. The educational campaign, which is a vital part of the whole program, is succeeding in having people, and more especially the women, seek diagnosis and

treatment earlier in the course of the disease, when the chances of cure are best. For example, among the patients at the cancer clinics in Massachusetts, the average delay between the first symptoms and visit to a physician was reduced from somewhat more than six months in the period, 1927 to 1935, to 3.3 months in 1943. If this accomplishment is not typical of the country as a whole, it at least has counterparts in many other clinical experiences.

The increasing control over cancer may also be attributed to a number of other factors. It is even likely that prevention has played some part. The close relation between cancer of the cervix of the uterus and neglected injuries at childbirth has been generally recognized. With the long-term fall in the birth rate and with marked improvements in obstetrical and postpartum care, the incidence of cancer of the female reproductive organs presumably has decreased. But far more important in the total picture, than prevention, has been the constantly increasing number of physicians trained to deal effectively with the disease, the marked increase in the public and private facilities for treatment, and the development of new and improved technique.

In conclusion I wish to acknowledge gratefully the help received from Dr. Lewis C. Scheffey in the preparation of statistical data used in this paper and for his criticism and advice.

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1827 SPRUCE STREET

THE CURABILITY OF GRANULOSA-CELL TUMORS

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AS GRANULOSA-CELL tumors have become more commonly recognized, it is apparent that the prognosis is more difficult to determine than formerly believed. It was at first thought that these tumors were benign. As the number of case reports multiplied and the follow-up studies were available, it became evident that the granulosa-cell tumor, although more benign than most other ovarian carcinomas, nevertheless carried with it a definite malignancy. The difficulty in the prognosis of the granulosa-cell tumor is further reflected by the wide variation of statements in the literature concerning its malignancy. The occurrence of malignancy among the granulosa-cell tumors is quoted by various authors as being as low as 10 per cent and as high as 55 per cent, with all intermediate gradations. The collection of adequate statistics on the malignancy of the granulosa-cell tumor is difficult as the incidence of late recurrence in this tumor group makes five- or even ten-year follow-up studies inadequate. This fact has been strikingly brought to our attention by the recent return of three patients to the gynecologic clinic, all having recurrent granulosa-cell tumors fifteen, sixteen, and nineteen years, respectively, after their original operation. These three cases are herein reported with accompanying photomicrographs of the original and the recurrent tumors.

Case 1.—R. G., No. 182937, a 39-year-old Negro woman, was admitted to the Johns Hopkins Hospital, June 13, 1923, with the complaint of abdominal swelling and some loss of weight during the past six months. Her past history and family history, as far as could be determined, were noncontributory. She had been married nineteen years and had had three pregnancies, the youngest child being 11 years old. The onset of menstruation had been at the age of 14 years with a 21-day-interval and a duration of three to four days. The last menstrual period was May 3, and the previous one April 5. For the past six months, since the onset of the present illness, she had had intermenstrual bleeding and profuse leucorrhea.

On physical examination the temperature was 99° F., pulse 84, respiration 40, and blood pressure 125/70. The hemoglobin was 68 per cent and the white blood count 7,200. There were signs of a right hydrothorax; the abdomen was extremely distended, and a nodular tumor mass, reaching 10 cm. above the symphysis, could be palpated. No definite fluid wave could be made out, but the percussion note was flat over the entire abdomen except for a triangle in the epigastrium. A pelvic examination showed the external genitalia to be normal, the cervix low in the vaginal vault, small, conical, and firm. The fundus seemed to be continuous with the abdominal mass and neither ovary was palpated as such. An x-ray of the chest confirmed the diagnosis of right pleurisy with effusion.

On June 15, 1923, a paracentesis was done and 4,000 c.c. of fluid removed. Analysis showed the ascitic fluid to have a specific gravity of 1.020 and a 4 plus albumin; no tumor cells were seen on microscopic examination. The paracentesis was repeated on June 17 and again on June 18, with the removal of 4,000 c.c. of fluid each time. On June 19 a thoracentesis was performed and 1,000 c.c. of fluid removed; this procedure was repeated on June 24.

On June 30 a paracentesis was again done, with the removal this time of 7,500 c.c. of fluid. A definite tumor mass which filled the pelvis could now be palpated. The patient was therefore operated upon, July 3, and a bilateral salpingo-oophorectomy and hysterectomy performed. On opening the peritoneum, a tumor, arising from the right ovary and reaching almost to the umbilicus, was seen. The mass was free except for a few adhesions to the posterior aspect of the broad ligament. There were no peritoneal or visceral implants and no visible evidence of metastases to organs or lymphatics. The left ovary was small and appeared to be normal as did the uterus.

The gross pathologic examination showed a normal uterus measuring 7.5 by 3.5 cm. with a smooth endometrial lining. The right ovary was converted into a mass measuring 17 by 10 by 12 cm., of firm consistency throughout except for one small cystic area. The tumor was well encapsulated and had a smooth, glistening surface, free from adhesions. At one end the capsule had apparently been torn. On section, the growth was found to consist of friable tissue loosely held together by fibrous bands. There were numerous small cystic spaces from pin size to 2 cm. in diameter. The one larger cyst previously described was filled with blood. The left ovary was not remarkable.

The microscopic picture of this tumor was found to vary from that of a cylindroid granulosa-cell tumor to a microfollicular type (Fig. 1). It was a solid tumor composed of small cells with prominent, dark-staining nuclei and very little cytoplasm. In areas these cells were arranged in cords, giving the appearance which has been described as the moiré silk pattern. In other areas the cells were arranged in sheets with abortive follicle formation and occasional pseudo-Call-Exner bodies. The uterine endometrium was autolized. No microscopic description was therefore available. The pathologic diagnosis made at the original examination was carcinoma ovarii.

The postoperative course was uneventful. On discharge examination there was no evidence of a recurrence of the hydrothorax and the ascites which had recurred was found to be greatly diminished. There was a small cystic mass in the cul-de-sac of Douglas which was thought to be encapsulated ascitic fluid.

The patient was next seen in the accident room, Oct. 10, 1939. She was then 56 years old and presented signs and symptoms of an acute intestinal obstruction. For one year she had had chronic obstinate constipation. During the past five days she had suffered from diarrhea and intestinal cramps. In the four days just prior to her hospital admission she had had no bowel movements, and directly before admission had become distended and had begun to vomit. A physical examination revealed classic signs of intestinal obstruction, and a laparotomy was immediately performed. The abdomen was filled with bloody ascitic fluid; the pelvis was choked by a soft multinodular tumor mass suggesting carcinoma in its gross appearance; there were numerous peritoneal implants. A biopsy was performed and the obstructed loop of bowel released. Her postoperative course was uneventful and she was discharged to be followed in the tumor clinic.

Urinary estrogen determinations showed approximately 70 R.U./24 hours or 140 R.U./1 total estrogens.*

The microscopic picture of the tumor biopsy was that of an insular or diffuse granulosa-cell tumor (Fig. 2). The cellular morphology was much the same as seen in the original tumor, but there was a more marked tendency for the cells to grow in solid sheets. In a few areas the trabeculated cordlike growth of the cylindroid granulosa-cell tumor was approached, but no microfollicular areas were present, and pseudo-Call-Exner bodies were very rare.

*The estrogen determinations were made on total 24-hour urine collections. The urine was acidified to Congo red paper and extracted three times with butyl alcohol. The butyl alcohol was distilled to dryness under vacuum and the residue taken up in 0.1 N. sodium hydroxide. This solution was neutralized and then hydrolized by boiling 10 minutes with 15 vol. per cent concentrated hydrochloric acid. The hydrolized solution was cooled and extracted five times with ether. The ether extract was evaporated to about a 5 c.c. volume and 5 c.c. of olive oil added. The remainder of the ether was blown off and the oil solution was then ready for assay.

The assays were performed on adult castrate rats which were known to respond to one gamma of estrone with an estrous smear. A single injection was given and the rats were smeared after 48 hours. Six or eight rats were used on each assay depending upon the amount of estrogen present in the solution. Only full estrous smears were read as positive.

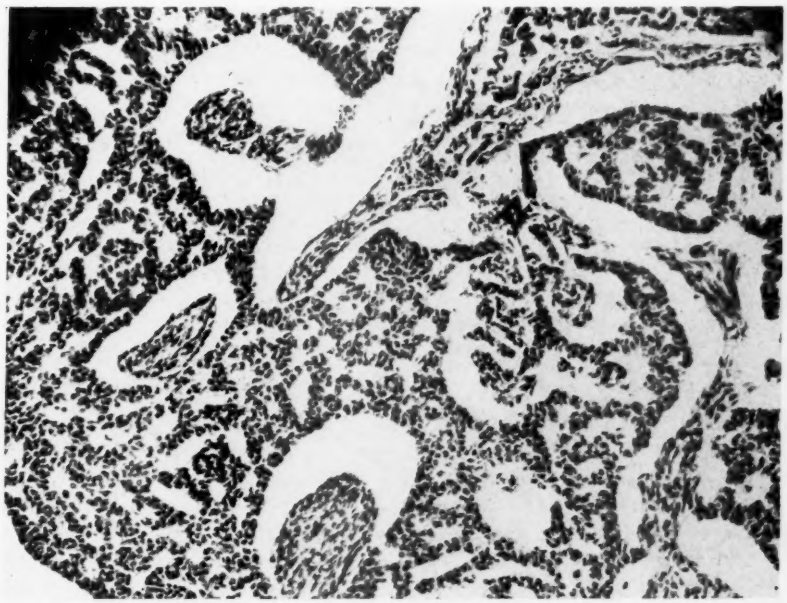

Fig. 1.—(Gyn. Path. No. 28681.) Low-power photomicrograph of original tumor removed from Case 1. This tumor shows areas typical of the cylindroid and microfollicular types of granulosa-cell tumor.

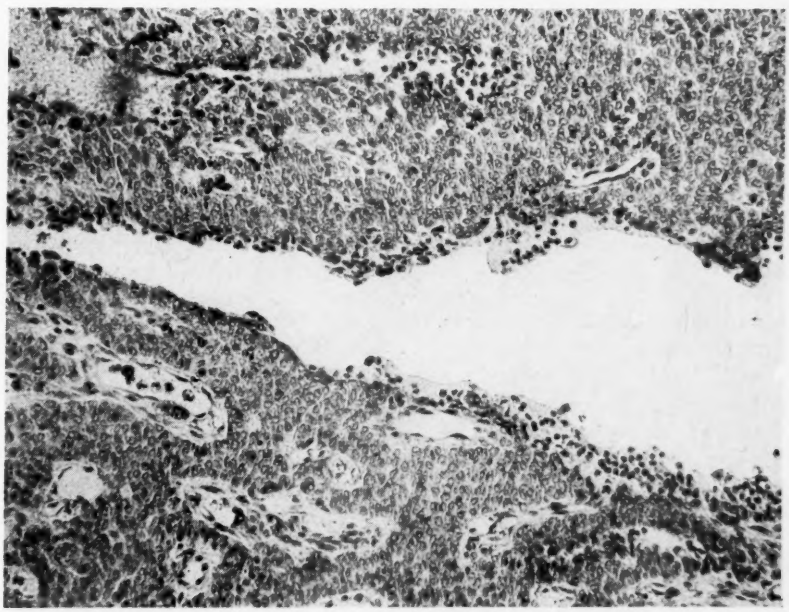

Fig. 2.—(Surg. Path. No. 75293.) Low-power photomicrograph of the biopsy removed from Case 1, sixteen years after the original operation. This tumor showed a more marked tendency to grow in solid sheets. However, there were definite cylindroid areas.

After a consultation in the tumor clinic, a course of x-ray therapy was given. She received 1,700 roentgen units through two 20 by 20 cm. portals at a skin target distance of 50 through a Thoreus filter (2 mm. Cu, 1 mm. Al). A 200-kv., 20-Ma. machine was used. Nine hundred roentgen units were given to a third portal, 15 by 15 cm., over the liver. The factors were the same as before. The entire course covered a period of three months.

When seen Jan. 31, 1940, there were no palpable abdominal masses and no ascites was present.

The patient remained free from symptoms until July 20, 1943, when she was again seen, complaining of generalized abdominal pain and anorexia of about one week's duration. The physical examination at this time showed recurrent abdominal and pelvic masses and ascites. A second course of x-ray therapy was deemed advisable, and from August 5 to October 12 she received a total of 1,000 roentgen units, using two pelvic portals, one anterior and one posterior, of 20 by 20 cm. each. The factors were 400 kv., 5 Ma. at 70 skin target distance, using a 3-mm. Cu and 1-mm. Al filter. There was no apparent improvement either symptomatically or objectively and the patient died at home May 18, 1944. No autopsy was obtained.

CASE 2.—E. D., No. 171029, a 56-year-old Negro woman, was admitted to the hospital, April 8, 1924, complaining of a painful swelling of the lower abdomen. Her family history and past history were unessential. She had been married thirty-three years and had one son aged 30 years. There had been one miscarriage at four months, two years after the birth of this baby and no subsequent pregnancies. Her menses had begun at the age of 15 years and had always been regular, appearing every twenty-eight days and lasting five to six days with moderate flow and no dysmenorrhea or leucorrhea. Two years before admission she had begun to have menses every two weeks, lasting from five to six days but with scanty flow. Her last menstrual period had begun on March 25, 1924. She dated her present illness to three years before when she first noticed a lump in her "stomach." For one year she had had bearing-down pains in the lower abdomen, and for the past six months had noted a rapid increase in the size of her abdomen.

On physical examination at the time of admission to the hospital, the hemoglobin was found to be 55 per cent; white blood cells, 5,140; temperature, 98° F., pulse, 80; and blood pressure 162/100. There was a large abdominal mass extending to within 2 fingerbreadths of the costal margin on the right and into the hypochondrium, with a slightly lower limit on the left. The surface of this mass appeared to be nodular; however, in the right lower quadrant it was somewhat cystic to palpation. In the midline and to the left there was a firm mass corresponding to a uterus enlarged to about twice normal size. This mass was freely movable from side to side. The pelvic examination showed the external genitalia to be normal. The cervix pointed anteriorly and was located just behind the symphysis. It was soft and patulous in consistency. The mass described on abdominal examination was noted as possibly an enlarged, myomatous fundus, although it was stated that the right ovary could not be palpated. There was a cystic mass in the cul-de-sac and a small mass on the left which seemed to be the left ovary. Numerous nodules extended into the lateral pelvic walls.

A hysteromyomectomy, bilateral salpingectomy, right oophorectomy, and partial left oophorectomy were performed, April 8, 1924. The mass described in the physical examination was found to be a large multinodular ovarian cyst. It was not adherent and was easily removed; however, one thin-walled locule was ruptured in the process. Grossly, the growth was a nodular tumor of the right ovary, with solid and cystic areas measuring 30 cm. in diameter. The cysts were of various sizes and colors, some smooth-walled and others lined with papillary projecting nodules. Interspersed throughout the cystic spaces were many firm, solid areas. There was no invasion and in every place the tumor seemed to be incapsulated. It was apparently entirely removed. When the microscopic appearance of this tumor was reviewed, it was found to be a typical microfollicular type of granulosa-cell tumor (Fig. 3). There were solid areas of small cells with dark-staining nuclei and relatively little cytoplasm. These cells were arranged concentrically about small cystic

spaces containing a pink-staining fluid. Call-Exner bodies were numerous. The uterine endometrium showed a hyperplastic pattern. The microscopic diagnosis at the time of the original examination was carcinoma of the right ovary arising in a cystadenoma.

The patient was discharged from the hospital after an uneventful postoperative recovery. It was not deemed advisable to give her postoperative irradiation.

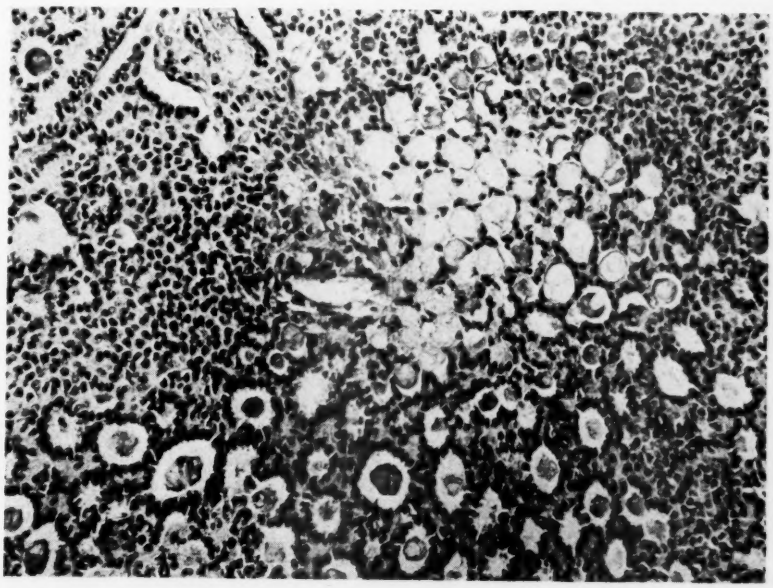

Fig. 3.—(Gyn. Path. No. 29319.) Low-power photomicrograph of original tumor from Case 2. The typical picture of the microfollicular granulosa-cell tumor is seen.

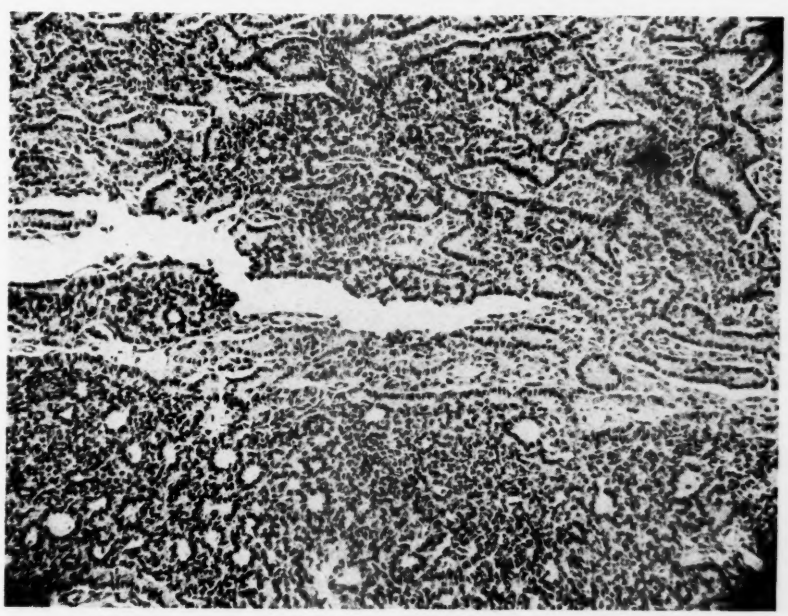

Fig. 4.—(Gyn. Path. No. 50609.) Low-power photomicrograph of the biopsy taken on Case 2, sixteen years after the original operation. The tumor again shows the typical picture of a microfollicular granulosa-cell tumor.

She was next seen June 1, 1938, at which time her only complaint was a painless "lump" in the "stomach" for one year. She was still actively employed as a cook and claimed to be in excellent health. She had never experienced menopausal symptoms and reported that she still maintained her libido. On physical examination the patient was found to be a small, well-preserved, vigorous Negro woman of 70 years. A mass, apparently originating in the pelvis and reaching to the umbilicus, was palpable. There were several small masses in the epigastric region, which were thought to represent liver metastasis. Two discrete nodules were palpable in the lower midline scar, measuring about 5 by 5 cm. in diameter. No ascites was demonstrated. The pelvis was choked by the tumor mass. The diagnosis of recurrent granulosa-cell tumor was made and at this time she was referred to the tumor clinic for advice as to x-ray therapy. Here it was felt that, in view of the apparent lack of symptoms and the questionable response of the granulosa-cell tumor to irradiation, the patient should not be treated. She was followed in the tumor clinic over a period of two years, during which time there was very little progress noted in the growth of the tumor masses. She was finally persuaded to enter the hospital for a biopsy of a tumor nodule. This was performed June 10, 1940, and urinary estrogen examinations were obtained concomitantly. The microscopic appearance of the biopsy was strikingly like that of the original tumor (Fig. 4). There were solid sheets of cells showing a tendency to form concentrically around small cystic spaces. Other areas approached the moiré silk appearance of the cylindroid granulosa-cell tumor.

The estrogen values in this case were calculated at approximately 500 rat units and 250 rat units of total estrogens per liter of urine. These values were obtained for specimens collected on two separate days. Unfortunately these were not calculated in terms of the twenty-four-hour period and so cannot be compared with the values obtained in the other two cases.

The patient continued to be seen in the dispensary every six months. She grew gradually more feeble and cachectic but never developed symptoms of acute intestinal obstruction. She remained fairly comfortable until her death, in September, 1942. The patient did not die in the hospital and no autopsy was obtained. As far as could be determined from the family, death was from inanition.

CASE 3.—L. M., No. 198364, a 26-year-old Negro woman, was admitted to the gynecologic ward, Oct. 30, 1920, complaining of an abdominal swelling and irregular menses. Her family history and past history were noncontributory. Menses had begun at 12 years of age and had been regular until about two years prior to her hospitalization. She had been married six years and had had four pregnancies, one normal delivery, one stillbirth, and two miscarriages, occurring in the order given.

The patient dated her present illness to about two years ago when she experienced a period of amenorrhea lasting about one and one-half years. In June, 1920, she began to bleed and continued to do so for three weeks with considerable loss of blood. In July, she bled about one week, approximately as profusely as a normal period, but following this she noticed some swelling of the abdomen and shortness of breath. She had no further vaginal bleeding until one week before entering the hospital. At this time she noticed a slight show of blood which continued until her hospital admission, Oct. 30, 1920.

On physical examination the blood pressure was found to be 135/95; white blood count, 8,000; red blood count, 3,500; hemoglobin, 45 per cent; and blood Wassermann, negative. The abdomen was markedly distended by an irregular mass which reached above the umbilicus but which could not be satisfactorily outlined because of the tenseness of the abdominal wall. There was marked bulging of the flanks, but no fluid wave could be elicited and the percussion note over the right flank was tympanitic. On vaginal examination the external genitalia were normal, the outlet was parous with good support, and Bartholin's and Skene's glands were negative. The cervix was small and firm, and visualization revealed no abnormalities. The uterus lay anteriorly and seemed to be somewhat enlarged. The tumor which had been felt on abdominal examination was found to arise in the pelvis and was thought to be ovarian in origin.

Operation was performed on Nov. 1, 1920. Following an escape of about 500 c.c. of bloody ascitic fluid, the tumor mass was readily visualized. It was purple in color, extremely vascular, and of a soft consistency. The growth was freely movable and was found to arise from, and entirely replace, the left ovary. The right tube and ovary appeared normal as

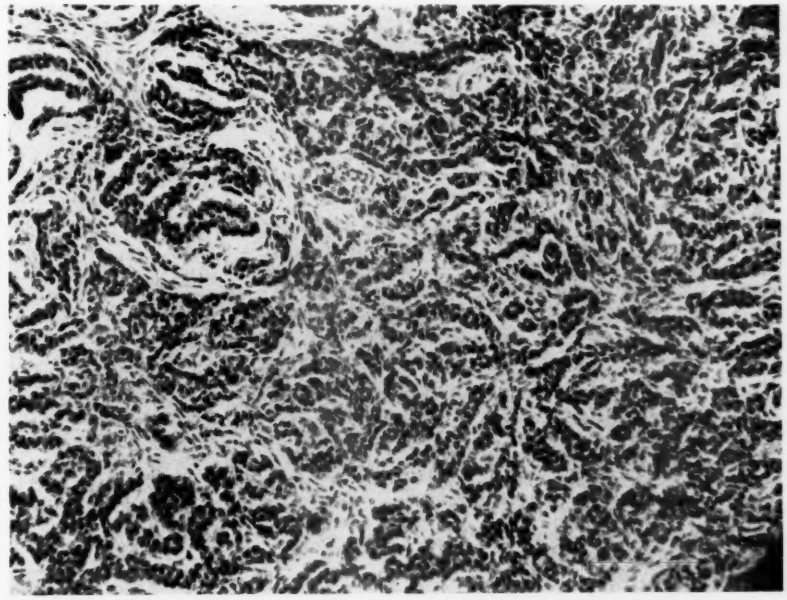

Fig. 5.—(Gyn. Path. No. 26320.) Low-power photomicrograph of the original tumor from Case 3. The cylindroid type of granulosa-cell tumor is seen.

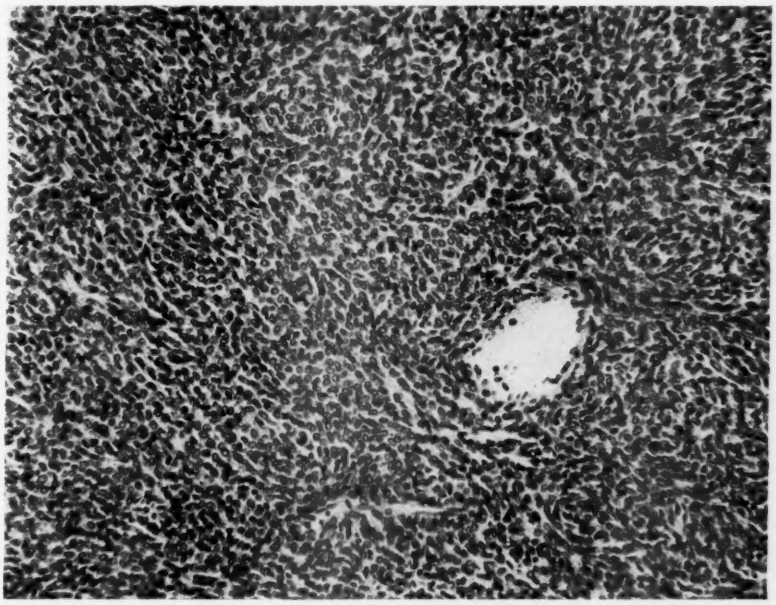

Fig. 6.—(Gyn. Path. No. 50505.) Low-power photomicrograph of the retroperitoneal tumor removed from Case 3, twenty years after the original operation. This tumor was very necrotic but the cellular area depicted represents the diffuse type of granulosa-cell tumor.

did the uterus except for a small myomatous nodule on the posterior surface. The tumor and the left tube were removed. No evidence of any ovarian tissue on the left side remained. The patient left the operating room in good condition, and the postoperative course was uneventful. She was discharged on Nov. 15, 1920, apparently well.

The pathologic report was as follows: The specimen was a tumor arising in and replacing entirely the left ovary, weighing 6,000 Gm. and measuring 28 by 25 by 15 cm. It had an irregular, nodular surface covered by a smooth, glistening capsule which was in no place broken. On section the growth was found to be in a large part solid with some cystic spaces. The solid areas were a mottled grayish-red in color and of soft consistency; it was trabeculated by fibrous tissue septa and there were numerous areas of degeneration. The cystic spaces contained clear fluid. The microscopic diagnosis at the time was adenocarcinoma in a multilocular cystadenoma. This tumor in retrospect was again found to have the morphology of a cylindroid granulosa-cell tumor (Fig. 5). It was largely a solid tumor composed of the small cell characteristic of the granulosa layer, arranged in cords running through a dense connective tissue stroma. In other areas these cells were in solid nests and in still others showed a tendency to form micro- and macrofollicular areas.

The patient was seen next in the dispensary in 1926, complaining of backache, and again in 1928 with a gastric disturbance. On neither occasion was there any evidence of recurrent disease in the pelvis.

On May 1, 1940, almost twenty years after her previous hospital admission, she was admitted to the medical service complaining of a "lump" in the right side. Three years previously her menstrual periods had ceased. One year ago she had noticed a slightly tender mass in the right upper quadrant near the umbilicus. This mass gradually increased in size until about three weeks before her admission to the hospital, at which time it began to grow rapidly. Six months ago her menstural periods had recurred, and she had had periods of vaginal bleeding about every fourteen days since then. Three months ago she consulted her family physician because of a loss of 45 pounds in weight over a period of one year. She was told at this time that she had diabetes mellitus and was put on a diet but given no insulin.

At the time of admission her temperature was 99.6° F.; pulse, 100; respiration, 20; blood pressure, 180/100. The blood examination showed a white blood count of 9,800, and a hemoglobin of 90 per cent. The fasting blood sugar was 182 mg. per cent, and blood Wassermann was negative. The basal metabolic rate was +26 per cent. On physical examination the heart was found to be enlarged. The liver was palpated 3 fingerbreadths below the costal margin and there was a mass in the right upper quadrant which seemed to be continuous with the liver edge. The pelvic examination was negative except for the presence of a few myomatous nodules on the uterus. The diagnosis was thought to be hypertension, arteriosclerosis, diabetes mellitus, and an abdominal tumor. The blood estrogen was 40 R.U./1, and the urine estrogen, 35 R.U./24 hours, and 25 R.U./24 hours, on two separate days.

After several weeks of bed rest, an exploratory laparotomy was performed. The mass in the right upper quadrant was found to be a retroperitoneal tumor, and a careful examination of the abdomen and pelvis failed to reveal any other site of tumor formation. The uterus was enlarged and nodular, and the right ovary was small and fibrotic. No tumor was palpable in the gastrointestinal tract and the kidneys were normal. The tumor mass was shelled from its capsule with relative ease but at the end of the procedure a considerable amount of blood was seen to be oozing from the former tumor bed. This bleeding was controlled by packing with two gauze rolls which were left in place when the abdomen was closed. During the operation the patient's blood pressure, which had been 210/90, dropped to a systolic of 80, and, in spite of stimulants and supportive therapy of 500 c.c. of citrated blood, failed to sustain a rise. She died two hours after her return to the ward.

The tumor was fragmented when it reached the laboratory and numerous sections were taken in various locations. Many microscopic areas showed only hyalinized or necrotic tissue, but others showed solid islands of small cells with dark-staining nuclei and very

little cytoplasm, resembling those seen in the diffuse type of granulosa-cell tumor and approaching also the more cellular areas of the sarcomatous granulosa-cell tumor (Fig. 6). Microscopically this tumor was not as typical as the others in the group.

(Autopsy No. 16924.) At autopsy there was a small amount of serosanguineous fluid in the peritoneal cavity, and the gauze packs which had been left in place at the operation were saturated, but there was no free blood present. The abdominal viscera were grossly normal except for the liver which showed a marked compression of the right lobe. This was apparently caused by the right retroperitoneal tumor mass which had been removed at operation. The left lobe was correspondingly hypertrophied.

There was no evidence of malignant growth in the pelvis or pelvic organs. The uterus was irregularly enlarged and there were a few small myomatous nodules in the walls. The lining was smooth. The right ovary was pale and atrophic looking.

The hypophysis was slightly enlarged.

Microscopic examination of the organs showed an estrogenic type of endometrium, which corresponded to an interval nonsecretory pattern. The left ovary was senile in type; there were no Graafian follicles present. The pancreatic islands were increased in number but no hyalinization was present. There was some atrophy of the thyroid gland with an increase in the fibrous tissue stroma. The adrenals and pituitary gland were normal.

Discussion

The three cases reported further demonstrate that the prognosis in individual cases of granulosa-cell tumors is most uncertain. In all three cases the tumors were considered benign at the original operation in spite of excessive fluid being present in the abdomen in two. They were well encapsulated and there was no evidence of metastasis or implantation; in only one case (Case 2) was there a rupture of a small cystic locule with the escape of serous fluid—a circumstance which might possibly be considered a factor in disseminating the process. All three patients were apparently well and healthy over a period of at least fifteen years, and yet all died of the disease eighteen, twenty, and twenty-one years, respectively, after the original operation.

Whether the second tumors represent true recurrences or are new neoplasms is an interesting theoretical question and one with some practical significance, as its solution might give us a clue as to the best method of treatment. If they are metastases or recurrences, then the first operation should be as extensive as possible and great care should be taken in handling the tumors in order to avoid rupture. If they represent new tumors and can occur anywhere in the pelvis, or indeed in the abdomen, where embryonic rests might remain, a simple excision of the original tumor might be as satisfactory as a more extensive procedure.

In Case 1, widespread metastases occurred after sixteen years in spite of a bilateral salpingo-oophorectomy and a hysterectomy. In Case 3, in which only a unilateral salpingo-oophorectomy was done, the second tumor was located in the right retroperitoneal space, leaving the remaining pelvic organs free. This corresponds to a case reported by Compton of a recurrent granulosa-cell tumor in the right vesicouterine fold, completely independent of the right ovary, sixteen years after the removal of the original left ovarian tumor. Such cases make it impossible to be didactic about the treatment of granulosa-cell tumors and lead us to the very pessimistic conclusion that, in certain in-

stances, no operative procedure, no matter how extensive, will assure the patient freedom from the disease later in life.

The urinary estrogen values on the cases reported were within the limits of normal values for cyclic women except for one value of 500 R.U./1, which is high. All of the values, however, were elevated for postmenopausal women as, in the departmental laboratory, values above 10 R.U./24 hours or 15 R.U./1 for such patients are unusual. Such relatively low values may indicate that there is a wide variation in the ability of granulosa-cell tumors to secrete estrogens. Although excessive amounts of estrogens were not produced, clinically physiologic estrogenic effects were manifested. In Cases 1 and 2, in which the uteri had been removed, the vaginae exhibited no evidence of senile changes: the mucosa of each was succulent and the rugae well formed. In Case 3, there had been a recurrence of uterine bleeding and the endometrium at autopsy showed an estrogenic pattern approaching a true hyperplasia.

Conclusions

1. Three cases of granulosa-cell tumors have been reported in which recurrences developed not less than fourteen years after the original operation.

2. All three patients have died, eighteen, twenty, and twenty-one years, respectively, following the removal of the primary tumor, in spite of the fact that the tumors were well encapsulated and showed no evidence of metastasis or implantation at the original operation. One case recurred in spite of a bilateral salpingo-oophorectomy and a hysterectomy.

3. One case, No. 3, with widespread inoperable abdominal metastases, responded well to deep x-ray therapy over a period of three years but a subsequent recurrence of the growth proved refractory to treatment.

4. Total urinary estrogen values were not extremely high in two cases but within the range of values for normal cyclic women. However, the values were well above those usually found in this laboratory for postmenopausal women, into which age group all three patients fell at the time of recurrence. All three cases exhibited clinical signs of estrogenic activity on recurrence of the tumor.

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DIET REGULATION AND CONTROLLED WEIGHT IN PREGNANCY

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DURING the past fifteen years a number of reports on the value of diet in pregnancy have been published. Most of the authors have been very conservative in their conclusions as to the value of diet in pregnancy. However, some have made extravagant claims as to the value of an "adequate" or "complemented" diet in pregnancy. According to these authors, some of the results of a proper diet are to either prevent or decrease the incidence of abortion, anemia, toxemia, prematurity, fetal abnormalities, stillbirths and neonatal deaths, and to increase the ability of the mother to nurse her baby.

We believe that a diet containing sufficient amounts of the essential foods, especially protein, vitamins, and minerals, will lower the incidence of anemia in pregnancy and, by placing the woman in a state of nutritive efficiency, increase the resistance to infection which may occur during pregnancy or the puerperium, and also reduce the amount of edema in certain types of toxemia through weight control. We do not know whether or not such a diet will have any or all of the results mentioned in the preceding paragraph and believe that more extensive studies are necessary before we make the changes in our prenatal care indicated by these diet studies. Prenatal care both in private and clinic practice is already very expensive. However, its value does not compare with good delivery care. It is not the actual number of prenatal visits made by the patient that are of value but how carefully the doctor evaluates the findings and institutes the proper treatment that are of importance.

If each patient is to be interviewed repeatedly by a dietitian, the cost of prenatal care will be increased. We admit an average of 266 new obstetric patients to our clinics each month and two dietitians should be available for proper supervision. Also, the cost to the patient may be increased. The cost of additional food for normal pregnancy diet was approximately $4.50 per month during the month of March, 1945, according to a report from the Home Economics Division of the Chicago Welfare Administration. Soldiers' and sailors' wives are given an allotment of $50.00 per month, but if they become pregnant no increase is given for the additional food presumably required by the pregnant woman. It is surprising that the Children's Bureau has not made provisions for this additional cost. The Home Economics Division of the City of Chicago Welfare Administration calculated that the minimal cost for food for

*The service of the dietitian is supported by a special grant from the Community Fund of Chicago, Inc., as part of the clinic nutrition project in which twelve clinics are participating. The nutrition project was planned by the Health Division of the Council of Social Agencies of Chicago.

TABLE I. CHICAGO LYING-IN HOSPITAL STATISTICS

DELIVERIES	HOSPITAL MORTALITY				ABORTION (%)	TOXEMIA (%)	ECLAMPSIA	
	MATERNAL (%)	MATERNAL (NO.)	TOTAL FETAL (400+ GM.) RATE PER 1,000 BIRTHS: STILL-BIRTHS	TOTAL FETAL (400+ GM.) RATE PER 1,000 BIRTHS: NEO-NATAL			(%)	(NO.)
1931-1941—27,321	0.177	(50)	22.6	20.3	4.2	8.6	0.28	(78)
1941-1942— 3,276	0.122	(4)	18.3	16.8		7.7+	0.15	(5)
1942-1943— 3,813	0.105	(4)	19.6	17.0		6.9+	0.05	(2)
1943-1944— 3,481	0.057	(2)	16.2	16.5	4.8	6.6+	0.03	(1)
1944-1945— 3,471	0	(0)	12.4	17.0	7.2	6.1+	0.03	(1)

Toxemia figures since 1941 have not been completely tabulated.

a pregnant woman living alone was $19.20 during the month of March, 1945. While the recommended foods are available and a market order may be given to facilitate purchasing, it cannot be expected that all patients will actually purchase the food recommended for this sum.

It is not our purpose to detract from the value of the previous reports but to examine them critically and to show that there are certain facts about obstetric statistics as well as about diet that must be kept in mind by anyone attempting to draw conclusions based on so many variables. For example, during the past year no maternal deaths occurred in our Service. Our dietitian has been advising patients during this period and one could attribute the lack of maternal deaths to this factor alone. We are quite certain that no one would be so rash.

Data in Table I list statistics from our hospital for some maternal and fetal conditions. These statistics over a period of years have shown marked decreases in the incidence of eclampsia and severe pre-eclampsia, in maternal and fetal mortality, and in other complications. We attribute these reductions to increased skill and knowledge of the staff and better supervision of the resident staff. If we compare our results for the past year with those of ten years ago, the differences are marked. Control groups must be large and must be watched as carefully as the experimental groups and by the *same* individuals.

The increased number of abortions on our service during the past two years is due to the inclusion of all incomplete abortions (formerly, only those patients who passed the fetus in the hospital were counted). The incidence is still less than the average reported in the literature because even if the patient is seen at six to eight weeks' gestation (which is very early) and aborts, but does not enter the hospital, no notation is made in the hospital statistics.

Data from some of the nutritional reports are listed in Table II. Attention is directed to the small number of patients in most of the groups, and yet conclusions are based upon these small groups which, if acted upon, would raise the cost of prenatal care. Where lives are concerned, cost should not be considered; but we have not reached that period in medicine in which cost is of no importance.

A preliminary report by the British Minister of Health in 1938 stated that among 4,446 mothers receiving special food, the puerperal death rate was 0.45 per cent; the maternal death rate from associated causes, 0.67 per cent; and the infant death rate (stillbirth and neonatal),

TABLE II. RELATION OF DIET REGULATION TO MATERNAL AND FETAL COMPLICATIONS AND MORTALITY

AUTHOR	NO.	ANEMIA (%)	TOXEMIA (%)	ABORTION (%)	FETUS (%)				MISCELLANEOUS CONDITIONS
					PREM.	S.B.	NEO.	ABNORM.	
Chicago Lying-in Hospital	39,709	12.0	8.3	5.6	6.9	1.81	1.68	0.57	
Dieckmann									Puerp. Inf.
Control	175	2.9	8.6	2.4	2.9	2.9		0	8.6%
Cereal	179	2.8	5.9	0	1.7	6.7		0	3.9
Vitamin A & D	98	3.1	14.5	0	3.1	2.0		0	5.2
Cereal + A & D	102	3.9	4.9	0	3.0	2.0		0	2.0
Tompkins			Pre. Tox. Ec.						Edema Av. Wt. Gain
Control	750		8.0 16.0 0.6		4.9	2.7	2.7		59% 14.1 Kilo.
Diet study	750		0 4.0 0		0	0	0.3		13 9.5
Ebbs						S.B.			Hb. Conc. %
Poor diet	120	28.6	12.6	6.0	8.0	3.4			11.5 Gm.
Good	70	21.6	7.8	1.2	3.0	0.6			11.9
Supplemented and good	90	16.1	9.1	0	2.2	0			12.1
Burke			Pre-eclampsia						Funct. Immature
Poor diet	36	1.0	44.0	0	14.0	20.0	3.0	25.0	22.0
Fair diet	149	0	8.0	0	5.4	0	0.7	0	0
Good-Excellent	31	3.4	7.0	0	0.5	0	0	3.2	0
People's League			Tox. Pre.						
England					*				
Control Primip.	1,512		31.7 7.4		23.9				
Diet study Primip.	1,530		27.1 5.4		20.1				
Control Multip.	999		21.8 5.2		24.2				
Diet Study Multip.	980		21.8 3.6		20.1				
Balfour			Mat. Mort. Tox.			S.B. & Neo.			
England Control	4,392		0.4			6.60			
England Diet study	5,364		0.25			5.54			
Wales Control	2,760		1.19			8.48			
Wales Diet study	3,797		0.95			6.56			

*Delivery before 40 weeks instead of 38 weeks.

Pre. = pre-eclampsia. Tox. = toxemia. Ec. = eclampsia. Prem. = premature. S.B. = stillbirth. Neo. = neonatal. Hb. = hemoglobin. Abnorm. = abnormalities.

5.4 per cent. Among 9,040 mothers not receiving special foods, the corresponding rates were 3.54, 1.33 and 8.3 per cent, respectively. Unfortunately, the Minister in a later note stated that the practical difficulties in the way of securing precise comparability between the contrasted groups are so great that it is unlikely that scientifically adequate conclusions could be reached.

The People's League of Health in England studied large groups of pregnant patients, giving the study group vitamins and minerals. The results reported in 1942 are listed in Table II. The decrease in the incidence of toxemia was not significant but it was for preeclampsia. A significant decrease in the premature delivery rate was noted (before the fortieth week). These latter figures would have more value had they been divided into periods, i.e., before 28 weeks, and 28 to 38 weeks.

Balfour reported in 1944 on the results of complementing the diet of large numbers of pregnant women in England and Wales with yeast and milk. The results are given in Table II. They show a significant decrease in the total fetal mortality for the study group. One wonders about the difference in fetal mortality in the control groups from neighboring towns, ranging from 63 to 96 per 1,000 births, and the high maternal mortality due to toxemia.

Tompkins stated that the incidence of toxemia was almost seven times greater in patients on a deficient diet. The stillbirth and neonatal rates were also much higher. His results, which he attributes to diet, would be far more significant if he had obtained diet records and given prenatal care to his control patients instead of selecting their histories from the hospital files.

The report by Burke and her co-workers is difficult to break down into the number of various complications. One wonders why there were no abortions in this study. All stillbirths, premature and functionally immature fetuses, babies with erythroblastosis, congenital heart and other anomalies, are classified in the "poorest infant" group. There were four patients with placenta previa with no fetal deaths, but if the series were larger there would be fetal deaths from placenta previa, from abruptio placentae, and from the accidents of labor which certainly cannot be charged to diet. The groups of good-excellent and poor diet are too small to warrant any conclusions. The fetal grouping is not warranted.

Burke and co-workers state: "Nutrition has not occupied a place of major importance as a part of prenatal care. The obstetrician's primary interest is not so much the health and development of the unborn infant as the health of the mother during pregnancy." Diet instruction, right or wrong, has been given by obstetricians to pregnant patients for over thirty years. The obstetrician is interested in having a live healthy mother and a live healthy baby. If he disregarded one or the other he would soon have no practice.

Extravagant claims had been made by several investigators relative to the decrease in fetal mortality in the hemorrhagic disease and intracranial injury group, resulting from the administration of vitamin K to the mother during labor. Potter compared the stillbirth and neonatal deaths and autopsy findings on our service for five consecutive years. The data are given in Table III.

TABLE III

	1940	1941*	1942*	1943	1944 (10 MONTHS)
Stillbirth	24.6	19.4	20.6	15.6	14.3
Neonatal	26.4	16.8	18.0	15.9	17.5
Total	51.0	36.2	38.6	31.5	31.8
Number of babies	2,710	3,093	3,517	3,768	3,475

*Parenteral injection 3.2 mg. vitamin K (2-methyl-1, 4-naphthohydroquinone, 3—sodium sulfonate) during labor.

Dr. Potter states: "Examination of the death rates for the two years during which vitamin K was given and for the following two years show almost identical rates for the first ten days of life, and a distinctly lower stillbirth rate in the control series." Had the rate

for 1940 been used as a control, the improvement would have been marked. Potter concludes: "From a study of this material it seems justifiable to conclude that the routine administration of vitamin K during labor in no way affected the infant mortality or stillbirth rate in the Chicago Lying-in Hospital."

Abortion.—According to Taussig, the incidence of abortion ranges from 10 to 40 per cent of all conceptions. The figures for our clinic are 5.6+ per cent. Mall, Streeter, Huntington, and Hertig have each reported that two-thirds of spontaneous abortions are associated with and probably due to extensive abnormalities of the fetus. The remainder are due to maternal causes, such as: anomalies of the uterus, tumors, systemic disease, abnormal implantations of the ovum, etc. Improper diet may be an important factor in the etiology of these causes, but positive proof is lacking. Dieckmann and co-workers reported that in their diet studies in pregnant patients, 2.4 per cent of the control group aborted; and none aborted in the three complemented diet groups (cereal; vitamins A and D; both). Since most abortions occur within the first three months, and since most patients do not come to the doctor until after the third month, it is obvious why most diet studies have such a low incidence of abortion.

Toxemia.—The incidence of toxemia varies throughout the United States (0.5 to 25 per cent) and throughout the world (0 to 28 per cent). The edema, proteinuria, hypertension, and associated symptoms may be due to pre-eclampsia, eclampsia, essential hypertension, or glomerular nephritis (acute or chronic). Our percentages for these conditions are 38, 4, 56, and 2 per cent, respectively. The average fetal mortality due to toxemia from various clinics is 16 per cent (9 to 26 per cent). Our fetal mortality is given in Table IV.

TABLE IV

		TOTAL FETAL MORTALITY (%)
Pre-eclampsia:	mild	6
	severe	17
Essential hypertension:	mild	7
	severe	27
Glomerulonephritis		58

Obviously, the fetal mortality depends on the type of toxemia and on the severity. Pre-eclampsia occurs most frequently in the first pregnancy and diet is certainly one factor. The fact that it rarely recurs indicates that there are other factors because the diet would in all probability be the same in subsequent pregnancies. Fetal death in patients with essential hypertension and glomerulonephritis is due to vascular lesions in the maternal placental vessels and it is difficult to conceive of any effect that diet could have on these vessels. There is a very definite connection between the incidence of toxemia and civilization. Eclampsia and pre-eclampsia either do not occur or are very rare in many native peoples. Dieckmann and co-workers reported that, in their complemented diet studies, two groups showed a significant decrease in the incidence of toxemia and one showed an increase. They attributed these inconsistent results to the small number of patients in each group.

Anemia.—The hemoglobin concentration is decreased in normal pregnancy, reaching a minimum figure at 26 to 34 weeks' gestation and then increasing, but not reaching nonpregnant values until some weeks post partum. If one uses nonpregnant standards, two-thirds of the pregnant patients are anemic. If one uses pregnant standards, 12 per cent of pregnant patients are anemic. Bethell has shown that if the pregnant patient has an intake of 50 grams or more of animal protein per day, the patient will not develop macrocytic anemia during pregnancy.

Hemorrhages.—Most dietary reports have not discriminated between the various types of hemorrhage occurring in pregnancy. Since the hemorrhage in placenta previa is the result of an abnormal implantation of the ovum, it is difficult to see how diet could play any part. The majority of the cases of abruptio placentae are associated with toxemia, and it is conceivable that the toxemia could be attributable to diet. However, these patients usually have essential hypertension, rarely pre-eclampsia.

Fetal Mortality.—Our uncorrected figures for stillbirths (400 Gm. +) for a ten-year period was 2.26, and for the past year 1.24 per cent. It is 0.92 per cent for fetuses weighing 1,500 Gm. or more. Similar figures for the neonatal mortality are 2.03, 1.70, and 1.2 per cent. In 51 per cent of the stillbirths and in 19 per cent of the neonatal deaths, it was impossible for either the obstetrician or the fetal pathologist to determine the cause of death. It is difficult to see how a proper diet could be an important factor in reducing stillbirths and neonatal deaths. If there is a constant decline in the fetal mortality, as is occurring on our Service, and if the percentages are small, it is obvious that great care must be used in the interpretation of results, even though the differences may be statistically significant.

Fetal Anomalies.—Animal experimentation has demonstrated that *extreme* diet deficiencies result in some animal species in fetal abnormalities. Heredity is still the important factor in the production of minor abnormalities (cleft palate, extra digits, etc.) in human fetuses. Major anomalies have an unknown etiology. Burke and co-workers attribute fetal abnormalities in the human being to diet deficiency although their group is extremely small.

Size of Baby.—The veterinarian has been able by selective breeding and diet to increase the weight and stature of various animals, but heredity is still the important governing factor. Burke and co-workers believe that they have been able to increase the weight and length of the baby by increasing the protein intake. One wonders whether, if the protein intake in their patients had been increased another 20 or 30 grams per day, the fetal length would have increased an additional 2 or 3 centimeters.

Skeleton and Teeth.—A marked and prolonged deficiency in calcium, phosphorus, and vitamin D before and during pregnancy will result in fetal rickets and in faulty fetal tooth development, as well as in osteomalacia in the mother.

Breast Milk.—The veterinarian has been able by careful selective breeding and diet controls of cattle to increase either the amount or fat content of milk. This has not been done in the human being. However, the quality of human milk has been shown to be affected by a deficient diet. The percentage of mothers

with adequate breast milk at discharge from maternity hospitals is disappointingly low, due in great part to lack of nursing care. Most obstetricians believe that if the patient had a proper diet during pregnancy and lactation and if adequate time for instruction in nursing and psychotherapy could be given by the nurses to each mother, three-fourths of the babies instead of less than half would be breast fed.

Weight.—We believe that the pregnant patient must have a proper diet, but this does not mean that she should have an unlimited caloric intake and as a result gain excessively in weight. The pregnant patient does not have to eat for two her own size. The diet must be increased during the last trimester. Data shown in Fig. 1 are taken from a report by Swanson and Iob who analyzed fetuses at various ages. It is obvious that the amounts of nitrogen, calcium, phosphorus, and iron required for fetal growth are minimal up to the twenty-eighth week and from then on increase markedly; but even at term the total amount required is not excessive. The figure also shows the average weight of the baby for the various calendar months and it is noteworthy that the fetus at twenty-eight weeks weighs only 1,045 grams. We believe that the pregnant patients should be fed in only needed amounts as an athlete is fed at the "training table"—not stuffed as if for a killing.

It should be noted that many of the diseases peculiar to pregnancy occurring in domestic animals are the result of civilization and/or overfeeding. The milk fever of cattle occurs only in thoroughbred stock and is due to the marked loss of calcium in the milk. A disease of pregnant ewes is due to overfeeding and lack of exercise. The same is true for rabbits.

Chesley has made an extensive study of weight changes in pregnancy and states that the average weight gain based on all the reports in the literature is 10.9 kilograms with a standard deviation of 4.9 kilograms.

I calculated in 1936 that the necessary weight gain due to the physiologic changes of pregnancy—fetus, placenta, amniotic fluid, uterus, blood volume, breasts, etc.—amounts to 6.7 kilograms. Chesley calculates from reports in the literature a gain of 6.2 kilograms for the same physiologic changes of pregnancy. He states that there is an additional gain of 7 kilograms for the patient's body and tissues, of which approximately 2 kilograms are due to stored nitrogen. We do not see any need for the additional 7-kilogram gain and are not certain what levels of nitrogen storage are necessary. We believe that there is no need for a total weight gain greater than 8 kilograms above the ideal weight. The first three months of pregnancy are characterized by either little gain or a loss of weight. The average weight gain for the remainder should then be a maximum of 225 grams (½ pound) per week.

Every patient whose total weight gain is over 10.9 kilograms does not necessarily have toxemia. Statistics do show, however, that the incidence of toxemia is increased in those patients who gain more than 13 kilograms. The total gain in pregnancy is not so important as the rate of gain. Patients who gain more than 0.6 kilograms per week have an increased incidence of toxemia, especially pre-eclampsia.

Bethell and co-workers state that with nutrition instruction a much smaller percentage of patients were overweight at term. One year later a considerably higher percentage were overweight, having paid no attention to diet in the interim. They also state that of most significance for the majority of overweight women is the fact that *pregnancy is the provocative or aggravating agent responsible for increased weight gains throughout life, leading to the well-known hazards of obesity in later years.*

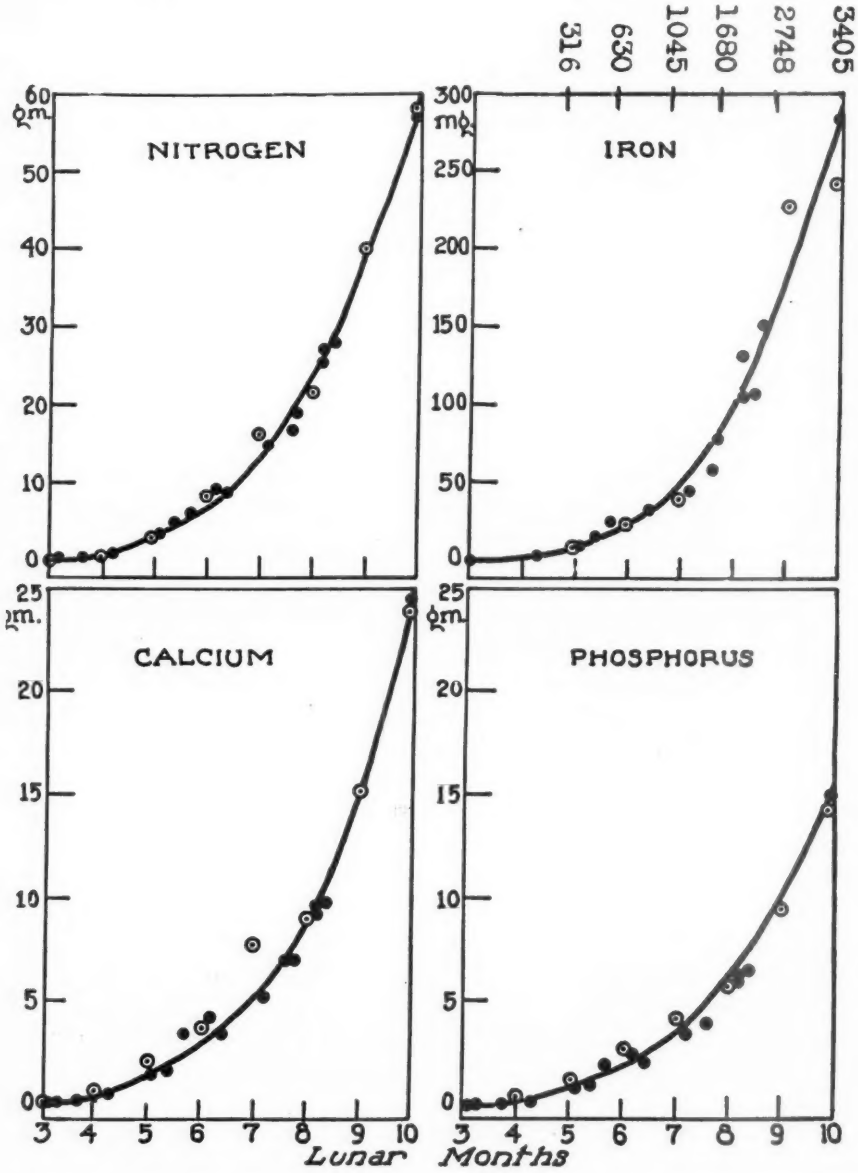

Fig. 1.—Shows the content of nitrogen, calcium, phosphorus, and iron, and weight of the fetus from the third to the end of the tenth lunar month. In all of the curves the authors' data are represented by the solid dot. (Modified from Swanson and Iob: AM. J. OBST. & GYNEC. 38: 382, 1939.

If the patient's weight is ideal before pregnancy, we believe that the maximum gain should be 7 to 8 kilograms. In order to aid the patient in limiting her weight gain, suitable dietary instructions have been developed. In the organization of a plan for practical use, a procedure has been developed whereby

TABLE V. APPROXIMATE EVALUATION[a] OF DAILY PLAN OF FOOD INTAKE FOR PREGNANCY, CONTAINING 1,800 CALORIES

	QUANTITY		MINERALS		VITAMINS					FOODSTUFFS			
DAILY FOOD INTAKE	WEIGHT (GM.)	APPROXIMATE MEASURE	Ca (G.M.)	Fe (MG.)	A (I.U.)	ASCORBIC ACID (MG.)	THIAMINE (MG.)	RIBOFLAVIN (MG.)	NIACIN (MG.)	CARB. (GM.)	PRO. (GM.)	FAT (GM.)	CALORIES[b]
Milk	960	1 quart	1.12	2.0	1,640	8	0.40	1.72	1.2	48	34	36	640
Egg	50	1 medium	0.03	1.4	495		0.07	0.18			6	6	80
Meat, poultry,[c] or fish, cooked	100[d]	Raw weight 4 oz.	0.01	3.3	2,807	2	0.28	0.37	5.9	1	24	13	215
Bread, whole grain or enriched	90	3 slices	0.03	2.0			0.24	0.13	2.6	45	9	3	240
Potato, cooked	100	½ cup	0.01	0.7	35	8	0.08	0.03	1.0	19	2		85
Green or yellow vegetable[e]	100	1 serving	0.10	1.4	4,870	23	0.05	0.17	0.6	6	1		30
Other vegetable[f]	200	2 servings	0.06	0.8	405	10	0.08	0.07	0.6	10	2		50
Legumes or beans: peas, navy, kidney, lima, or soybeans, or peanut butter	100	½ cup cooked	0.03	2.4	20		0.14	0.06	1.8	19	7	3	130
	50	¼ cup											
	25	1½ tablespoons											
Citrus fruit	200	1 cup juice	0.04	0.8	360	84	0.14	0.06	0.4	22	2		95
Other fruits[g]	100	1 serving	0.02	0.6	161	5	0.05	0.05	0.4	15	1		65
Butter or enriched margarine	15	3 level teaspoons			480							12	110
Coffee	25	2 tablespoons					0.04	0.01	2.3				
Sugar	15	1 tablespoon								15			60
Vitamin D concentrate[h]													
Total			1.45	15.4	11,273	140	1.57	2.85	16.8	200	88	73	1,800

[a]Figures on nutritive content taken from "Food Composition Table for Short Method of Dietary Analysis (Revised)" by Eva G. Donelson and Jane M. Leichsenring, J. Am. Dietet. A. 21: 440, 1945; and "Tables of Food Composition Giving Proximate Mineral and Vitamin Components of Foods," and "Tables of Vitamin Losses in Cooking of Foods," Committee on Food Composition of Food and Nutrition Board, National Research Council, 1944.

[b]Calories have been rounded off to nearest 5.

[c]The evaluation of meat is based on the use of 100 grams of liver, 250 grams of pork or ham, 150 grams of fish, and 500 grams of beef, veal, lamb, or fowl per ten-day period.

[d]Weight after cooking.

[e]The vegetables included in this group are asparagus, broccoli, carrots, green beans, kale, spinach, turnip greens, and other greens.

[f]The vegetables included in this group are: tomato, fresh, canned, or juice; vegetables commonly served raw as celery, cucumber, lettuce, and cabbage; and other cooked vegetables as beets, eggplant, onions, rutabagas, and cauliflower.

[g]All fruits except citrus have been included in this average.

[h]400 to 800 I. U. of vitamin D are given, the actual amount depending upon the concentrate used.

it is possible to note the value and use of each food which composes a plan of daily food intake containing 1,800 calories. By making appropriate adaptations of this basic plan, it then becomes possible to formulate diets suitable for variations in size, age, activity, cost, and food habits. In all cases, however, an attempt is made to limit the weight gain. The daily plan of food intake containing 1,800 calories is enumerated and evaluated in Table V.

In view of the present rationing restrictions and food shortages, complete instructions concerning food alternates have been necessary, particularly for the protein-containing foods. The restrictions on fat have been more of an advantage than a disadvantage because of the need for caloric limitations. Table VI outlines some of the suggestions given as alternates for the protein-containing foods.

TABLE VI. PROTEIN ALTERNATES RECOMMENDED IN DIET FOR PREGNANCY

DAILY FOOD INTAKE	APPROXIMATION OF PROTEIN CONTENT (GM.)
32 oz. (1 quart) of fluid milk The approximate protein equivalent of 1 pint of fluid milk is 8 oz. of evaporated milk or 1½ oz. (5 level tablespoons) of dried skim milk. Also, 1 serving (4 oz.) of milk pudding* or ice cream* may be considered approximately equivalent to 3 oz. of fluid milk.	34
One egg or 1 oz. of American cheddar-type cheese or 1 oz. of cottage cheese or 1 oz. of fish, poultry, or meat, or 1½ tablespoons of peanut butter†	6
4 oz. serving of meat or poultry or fish, or 2 oz. of soybean flour, or 7 oz. (1 cup) cooked soybeans, or 2 eggs and 2 oz. of cottage cheese. Also, 1½ tablespoons peanut butter may be considered equal to 1 oz. of meat.	24
3½ oz. serving (½ cup) of cooked peas, navy beans, kidney beans, or lima beans, or ¼ cup cooked soybeans, or 1½ tablespoons peanut butter	7
3½ oz. serving of potato, cooked	2
Other vegetables—3 servings	3
Citrus fruits—2 servings and one other fruit	3
3 slices of bread, enriched or whole grain, or equivalent grain product The approximate protein equivalent of one slice of bread is 1 oz. (dry weight) of cereal or ½ cup cooked spaghetti* or noodles* or 6 soda crackers, or 1 small piece of cake,* or a 2 inch cube of cornbread,* or 3 graham crackers.	9
Total	88

*Where variations in caloric values occur, adjustments are made to maintain isocaloric values.

†Twelve grams of dried brewer's yeast (3 level teaspoons) or twelve grams of peanut flour also yield six grams of protein.

When the patient is not accustomed to drinking milk, recommendations may be made, as suggested by Turner, for "the use of milk in soups, desserts, or flavored beverages. However, the most inconspicuous and in many cases, the most acceptable way in which to add milk is in the form of dried milk. Approximately 1½ ounces (5 tablespoons) of dried skim milk will equal one pint of fluid milk. This dried milk may be incorporated as a dry ingredient in the preparation of meat loaf, mashed potato, sandwich spreads, cooked cereals, hot breads, cookies, pastries, or puddings with little difficulty. Also, a palatable drink may be prepared by adding approximately 2½ tablespoons of dried milk to one glass (8 oz.) of fluid milk. This will provide approximately 15 Gm. of high quality protein per glass. In some parts of the country, dried milk may be obtained from the retail grocery store. In other places it may be necessary to depend on the courtesy of a bakery shop, hospital, or dairy."

Turner also pointed out that "milk contributes the major portion of calcium and phosphorus in the diet as well as a large share of the protein and vitamins of the B complex.

While 2½ ounces of cottage cheese would be equivalent in protein content to one pint of milk, the cottage cheese would supply less than one-tenth of the calcium, phosphorus, iron, vitamin A thiamine, and riboflavin supplied by the milk. Two and one-half ounces of American cheddar cheese would supply calcium equivalent to one pint of milk but would be much lower in vitamins of the B complex. In this case, the further use of liver or other glandular meat one or two times a week would be desirable to augment the iron and A and B vitamins in the diet. Pork would enrich the thiamine intake. Eggs will supply a significant amount of vitamin A and iron. Legumes and whole grains will also contribute iron and vitamins of the B complex." A comparison of the nutrients in equivalent amounts of protein-containing foods may be found in the table by Turner. Where any alternates or substitutions are used on the basic plan of food intake an attempt must be made to compensate for all nutrients.

The normal pregnancy diet as discussed is presented to the patient either in class or in an individual interview. Because of the large number of patients in the clinic, no attempt has been made to follow up these instructions unless the patient needs additional help in making certain dietary restrictions. The dietitian is always available for consultation with patients.

Lactation.—The increased requirements for lactation, over the needs for pregnancy, may be met simply by including an additional pint of fluid milk or equivalent (see Table VI), an additional serving of citrus fruit, and two tablespoons peanut butter or equivalent. Other foods may be used to supply these increased needs, by considering the total nutrient content of each food and making adequate use of compensatory foods.

We plan to make an evaluation of the dietary instruction by an intensive study of a part of this group of patients, through a correlation of the dietary intake with the laboratory and clinical findings. In an effort to increase the reliability of the diet history, it is planned to make a periodic record of the weight of the patient's food intake. It should then be possible with corresponding laboratory and clinical findings to determine if a correlation exists between nutrition and the incidence of toxemia, anemia, and the other factors previously mentioned.

Summary

The relation between diet in pregnancy and maternal and fetal complications and mortality has been discussed. The data so far reported in the literature indicate the value of a proper diet. The results, if true, are of the greatest importance, but the number of cases in each series is small. Furthermore, some of the conclusions are at variance with clinical obstetrics. The cost of supervising pregnant patients as well as supplying diet deficiencies would be increased but would be justified if the reports are confirmed. Therefore, we believe that research projects in maternal nutrition should be started in various clinics throughout the country so that in a short period of time sufficient material will be available.

We are limiting the total gain above the ideal weight to a maximum of 8 kilograms by restricting the caloric content of the pregnancy diet.

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GOVERNMENT AND MATERNAL WELFARE

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THE well-known phrases that each citizen of our country is guaranteed the fundamental rights of "life, liberty, and the pursuit of happiness," and that our government is "of the people, by the people, and for the people" are purposeless unless certain fundamental objectives are attained. Without a satisfactory economic base and a workable and responsive political and social system, these desiderata are not obtainable. Governmental authority must be derived from the people, be exercised by the people, and be for the benefit of the people.

Knowledge is the source of the power of the people and it must be based upon the truth. The fullness of life, the preservation of liberty, and the attainment of happiness depend upon education and health. These are very intimately interwoven. The meaning of these words is not to be interpreted in a narrow sense but broadly in their full application to body, mind, and soul. This cannot apply to the few if democracy is to succeed but must rest upon the freedom of equal opportunity for all to acquire the knowledge and health essential to their well-being. It must be recognized that, while each one of us is entitled to as nearly equal hereditary and environmental opportunities as it is possible to have, nevertheless we are not all alike in our bodily, mental, and spiritual powers. It is neither essential nor desirable that we should be, for life is too many-sided and complex for all of us to fit into the same groove. The comforts and pleasures of life are increased by the products derived from the diverse talents of others. However, we should have the personal optimum of knowledge and health to secure the maximal pleasure, happiness, and benefit from the manifold opportunities of life. Our Government can and should provide the opportunities, but the individual must supply the initiative, the time, the energy, and the ability. Unless these opportunities are forthcoming, it would seem that democracy could not succeed.

Our Government was founded upon the ideal of local self-government extended to progressively higher levels through systems of representation. The ideal would seem to be a maximum of local self-government with a minimum of centralized governmental control. In our extensive country with its great variation in available resources and wealth as well as in concentration and diversity of the population, there are manifold local problems which have to be solved largely by the intelligent interest of the local citizenry which frequently may need assistance from governmental agencies at higher levels.

The problems are not the same in all communities, and the methods of their solution differ. The abilities of the local leaders are not always equivalent. The total and the per capita cost would not be the same in every area even for identical plans. The available wealth also varies so that all communities would not be able to carry out programs to give their citizens the essentials of health and knowledge, and balance their budgets. This of course

means some assistance from outside. Other types of help would also be necessary as competent personnel must be available for various activities in devious capacities. All this implies the development and establishment of some plan for the equalization of the distribution of wealth and personnel so that these essential opportunities for the attainment of health and knowledge may be available for all.

Inasmuch as all of us are vitally affected by these programs, it behooves each one to scrutinize carefully all plans, especially those which involve our special activities and alter our ideals of democratic government. Various groups are particularly concerned, and it is important to recognize that the manner in which the individual is affected also is reflected in the group and reacts on the community for better or for worse. Those who are most familiar with the work of the groups in special fields should be the best informed and most capable of judging the results not only upon the workers themselves but also upon the segment of the community which they serve.

Before discussing problems concerning health it may be well to discuss those concerned with education because these have been more fully developed and determined on a national scale. We probably would all agree that in this field there has not been an equal opportunity for all of our prospective citizens. There are many factors which are responsible for this, one of which is the lack of sufficient wealth in some areas with which to provide the educational facilities and personnel. We have developed, side by side, a public school system, from preschool to higher levels of learning, and private and secular institutions with diverse means of support which meet a variety of needs and desires. All this has been accomplished through individual, local, and group initiative and enterprise, with a modicum of centralized governmental leadership or support. There are some serious gaps which need to be filled, many of which could be bridged by Federal, State, or local governmental subsidies.

A word about taxation may be pertinent. One could be justified in believing that two of the main purposes of Federal and State taxation should be: first, the support of the centralized government; and second, the equalization of the distribution of monies to secure to each community the essential opportunities to secure health and knowledge. This, according to our democratic principles, should be accomplished with a minimum of centralized control and a maximum of local initiative and accomplishment.

The development of health agencies is not exactly comparable to that of those devoted to education, as their local development has not been nearly as widespread. This is in part due to the more recent recognition of the essentiality of community health agencies. It appears that there is a much more pronounced tendency to centralized Federal initiative, support, and control through funds distributed to the States according to bureaucratic planning. It should be stressed that these tax funds come from the communities in varying ratios but are distributed mainly on the basis of matching and on a per capita basis. It is also important to recognize that of the total national income only a certain percentage could ever be available for taxation without wrecking our social and economic structure and, further, the larger the percentage

which goes into the Federal budget, the less there will be for State and local governmental budgets. If this plan is carried too far, it would practically destroy local self-government. It behooves us, therefore, to give careful consideration to governmental trends in these directions and interpret them not only in their relation to health activities but also to the development and protection of our democratic ideals.

Among the fields of health activities, that pertaining to maternity and infancy has great appeal, as there is not only an intelligent but also a sentimental interest, and often the emotions dominate the intelligence not only of individuals but also of the masses.

The Children's Bureau of the Department of Labor is a good example of the trend of the Federal Government in its health legislation and administration. Its activities, furthermore, have been more or less within the domain of health of mothers, infants, and children. In studying trends one can gain rather exact and pertinent information from studying the records which are to be found in the Annual Reports of the Secretary of Labor.

Originally approved by Congress on April 9, 1912, the Children's Bureau was in the Department of Commerce and Labor with Julia Lathrop as Chief. It was transferred to the Department of Labor upon its creation on March 4, 1913. This Bureau has had a life span of thirty-three years with three chiefs, Grace Abbott and Katharine Lenroot following Julia Lathrop. The original expressed purposes of the Department were "to foster, promote and develop the welfare of the wage earners of the U. S. A. and improve their working conditions and to advance their opportunities for profitable employment."

The stated purposes of the Bureau were to "investigate and report upon—all matters pertaining to the welfare of children, child life among all classes of our people, and shall especially investigate the question of infant mortality, the birth rate, orphanage, juvenile courts, desertion, dangerous occupations, accidents and diseases of children, employment legislation affecting children in the several States and Territories." In the first report it is stated that four bulletins were published, viz., on birth registration, urban baby saving campaigns, prenatal care, and statistical report on the number, age, sex, etc., of children. At this time the staff consisted of 15 persons, and the budget was $25,640 with $4,000 as a contingent fund.

The following year it was recommended that the staff be increased to 76 and the appropriation to $164,640. There were studies on infant mortality and the problem of mothers' pensions received attention. There were in addition other studies which had no bearing on maternal welfare. In 1915 a divisional organization was established consisting of (1) statistical, (2) library, (3) industrial, (4) hygiene, and (5) social service divisions.

In 1916 three new approaches for the development of the programs were stated: (1) studies in child welfare in rural areas by field workers; (2) research study of existing data on maternal mortality; (3) nationwide observance of "Baby Week." An increase of staff to 133 persons and an appropriation addition of $187,520 to make a total of $352,160 was recommended. The following purposes were stated: (1) continuance of the infant mortality

study; (2) development of rural studies of maternal and child welfare; (3) development of child labor studies.

In 1917 an administrative division was added for the enforcement Of the United States Child Labor Act, and Grace Abbott was made the Director. There was a special appropriation for this purpose. As the result of some studies in our own and other countries it was determined that the conservation of infant life was to be accomplished by "public protection of maternity"; the making "promptly and uniformly available, for all mothers and children, in town and country alike, irrespective of income, the services of nurses, doctors, conference centers and hospitals." The "Children's Bureau recommends the adoption in the U. S. A. of a nationwide plan for the public protection of maternity with Federal aid." The suggested program was to include not less than: (1) Public Health nurses, (2) instruction in schools and universities, (3) conference centers, (4) hospital facilities, (5) proper care at childbirth.

In 1918 the report stressed the public protection of infancy and maternity, cited statistics concerning the relation between family income and infant mortality, quoted mortality figures for mothers and infants and the relationship between maternal care and infant mortality, and pointed out the failure to reduce mortality since 1900.

In 1919 a special allocation of $150,000 was received from the President's Fund, and certain minimal standards for maternal care were set forth. These included:

1. Sufficient available maternity or prenatal centers to provide for all cases not otherwise receiving such care. Certain standards of care were elaborated.

2. Accessory clinics for pregnant women such as dental, venereal, etc.

3. Maternity hospitals or maternity wards in general hospitals sufficient to provide care in all complicated cases and for all women wishing hospital care; free or part payment for obstetric care in every necessitous case at home or in a hospital.

4. All midwives to have adequate training, to be licensed and supervised.

5. Income sufficient to allow the women to remain home during lactation.

6. Education of the public relative to the importance of problems presented by infant and maternal mortality and their solution.

The funds available during that fiscal year had been increased to $597,160.

In 1920 an appropriation of $654,260 was requested for the ensuing year. The report called attention to the fact that before the campaigns of the Children's Bureau only eight States had child hygiene or welfare divisions and that now there were 35. An interesting statement is made in this report: "One of the bureau's most important functions in the field of child health is the service it can render in an advisory capacity to these newly created divisions." For the fiscal year ending June 30, 1921, the expenditures of the Children's Bureau were $238,383.

It was in November, 1921, that the so-called Sheppard-Towner Act became law. During that fiscal year the expenditures, $236,751, and an additional $204,638 were transferred to the States. This Act specifically required that there was to be no payment to the mother, and none for buildings or equipment.

In 1923 the report says, "The Children's Bureau created in 1912 for scien-

tific research in the field of child care has had its usefulness greatly extended during the past year by the passage of the Maternity and Infancy Act."

In March, 1922, the appropriation for the purposes of the above Act was $490,000. Of this, $12,500, about 2½ per cent, was for administration; $240,000 was to be equally divided among the States; and the remainder, $237,500, was to be apportioned according to population and matched.

Quoting from the report of that year one finds interesting sentences:

"The specific measures involved in State plans are accurate birth registration, improved milk supplies, State surveys of the medical and nursing facilities for maternal and infant care, and registration and supervision of midwives. Everywhere the plans of work are largely educational to be carried out through actual teaching of mothers by public health nurses." "Any public health measure is largely educational." "This is particularly true of maternal and child hygiene."

In 1923 the constitutionality of the "Act," which had been questioned by Massachusetts, was upheld and forty States had accepted the programs. In 1922, $477,500 were available to the States, and in 1923, $1,190,000. The report in 1924 indicates that "during the last year real progress has been made by the States both in developing programs especially adapted to local needs and in extending the educational work to a larger number of mothers."

In the report of 1925, the Children's Bureau expended $342,873, and the funds available for 43 States and Hawaii amounted to $477,500 available from 1922, and $1,190,000 for the fiscal year 1923-1924. The specific objectives mentioned were "better care through the teaching of mothers and their education relative to the need and value of skilled supervision during pregnancy, child birth and the lying-in period and more widespread medical and nursing facilities so that adequate maternity and infancy supervision will be available to all who need it."

In 1926 the *Standards of Prenatal Care* were published, and by 1927 two additional States had accepted the provisions of the Act leaving Massachusetts, Connecticut and Illinois as the only exceptions. The five-year appropriation of $1,240,000 annually ended on June 30, 1927, but special legislation extended it for two years, i.e., until June 30, 1929. The annual report argues that "Any unprejudiced examination of the work done under the Act would show the value of cooperation of Federal, State, and Local Governments in developing better home care for mothers and babies and better community provision for hospital care at the time of child birth." The expenditures of the Children's Bureau were $337,878, not including the allotments to States.

In 1928 the funds available for the States were $1,201,725 and the expenditures of the Children's Bureau were $317,339. The following quotations are pertinent. "In the 16 years that it has functioned as a fact-gathering bureau, public and private agencies interested in the care of children and individual parents have increasingly made use of the information that has been painstakingly and dispassionately assembled by the scientific staff of the bureau."

It is noted in the 1929 report that "The Sheppard-Towner Act, which was approved Nov. 23, 1921, provided for Federal and State co-operation in promoting the welfare and hygiene of maternity and infancy for a five year period. This was later extended for another two years and by 1929, 45 States and the Territory of Hawaii were co-operating with the Children's Bureau

under the Act. It was the obvious intent of Congress in enacting the law that the Federal Government should lead the way in providing for the better care of mothers and children of the nation and to that end it made generous appropriations from the Federal Treasury for use in the States which made like appropriations for the same purpose." "Although Federal Funds are no longer available for actual participation it is the purpose that the Children's Bureau shall continue its recognized leadership in the maternity and infancy work in collecting and publishing helpful information as well as in an advisory capacity." The expenditures were $316,274.

The report of 1930 indicates the conclusion of the field work on the maternal mortality study begun in 1926 in 15 States. Also progress in the study of the causes of stillbirths and neonatal deaths. Important steps were taken in July, 1929, in planning the work of the Hoover "White House Conference on Child Health and Protection" which was financed by other than government funds. This conference had an important Subcommittee on Prenatal and Maternal Care as part of the Section I Medical Service which held its final sessions in February, 1931. As a result, *The Children's Charter* was promulgated, from which the following excerpt is taken: "The right to grow up in a family with an adequate standard of living and the security of a stable income as the surest safeguard against social handicaps."

The reports of 1931, 1932, 1933, and 1934 show expenditures of $338,865, $386,632, $359,183, and $343,241, respectively. The *Maternal Mortality Report* was published in 1933, and in 1934 emphasis was placed upon the great need for Federal cooperation with the States along the lines of the previous Maternity and Infancy Act.

The expenditures in 1935 were $342,631. The report of that year points out that with the "enactment of the Social Security Act of August 14, 1935, and the appropriation of funds to make it operative Feb. 11, 1936, a far-reaching specialized undertaking to safeguard the health and welfare of America's children was inaugurated."

The 1937 report shows the expenditure of $6,704,024, of which the allocation to States was $213,176 in 1936, and $2,788,608 in 1937 for carrying out the maternity and infancy program and a comparable but somewhat smaller amount for the care of crippled children. Quoting, we find that "evidence is steadily accumulating that a direct and courageous attack must be made on the central problem of reducing maternal mortality and morbidity and deaths of infants under one month by extending adequate medical and nursing care to all mothers and infants at the time of delivery and by continuing medical and nursing supervision throughout the prenatal and postnatal periods." At this time the appropriation under the Social Security Act was:

Maternity and Infant Health Service	$2,820,000
Crippled Children	2,150,000
Child Welfare	1,200,000
Federal Administration	299,000

The report of 1938 indicates a total appropriation of $8,352,359.

In July, 1938, the National Health Conference's "recommendations in the

fields of maternal and child health called for a gradually expanding program reaching at least by its tenth year a total additional expenditure of $165,000,000 distributed as follows:

Maternity Care and Care of Newborn Infants	$95,000,000
Medical Care of Infants	60,000,000
Services for Crippled Children	10,000,000

The Federal Government was to meet approximately one-half by the Social Security Act Appropriation.

In this annual report these appropriations are listed as:

Maternity and Infancy	$3,700,000
Crippled Children	2,800,000
Child Welfare	1,475,000
Administration	306,000

The annual reports of 1939, 1940, and 1941 indicate expenditures for the respective years of $8,964,927, $10,618,693, and $11,935,944, and in 1942 emphasis is placed upon "the need for public provision for maternity care for wives of men in the armed services and medical care for their children."

During that year the payments to the States were:

Maternity and Infancy	$5,983,318
Crippled Children	4,053,292
Child Welfare	1,569,009

The 1943 report shows the following expenditures:

Maternity and Infancy	$5,740,218
EMIC*	1,200,000
Crippled Children	3,862,531
Child Welfare	1,582,774

In 1944 the report indicated payments to the States as follows:

Maternity and Infancy	$ 5,946,183
EMIC	29,700,000
Crippled Children	3,781,751
Child Welfare	1,423,314

"This new program has contributed to the development of improved standards of maternal and infant care and has stimulated widespread interest in developing additional resources for medical, hospital and nursing care."

There is now before Congress a bill entitled Maternal and Child Welfare Act of 1945. Under Title I, its purposes are enumerated as follows:

1. Maternity care, including medical, nursing, dental, hospital, and related services.
2. Preventive maternal and child health work, including mental health.
3. School health services.
4. Diagnostic services and care of sick children, including medical, nursing, hospital, and related services.
5. Dental care of children.
6. Correction of defects and conditions likely to interfere with normal growth and development and the educational progress of children.
7. Demonstration projects in the field of maternal and child health.
8. Training of professional and technical personnel.

*The Emergency Maternity and Infant Care appropriation was $4,400,000.

The appropriation of $50,000,000 is authorized for the fiscal year ending June 30, 1946.

Under Title II, $25,000,000 is appropriated for the care of crippled children.

Under Title III, there is an appropriation of $20,000,000 for child welfare. The approval of all State plans are vested in the Chief of the Children's Bureau. All plans are to be in accord with Title V of the Social Security Act. "To carry out these functions and to administer the programs provided for under this act, $5,000,000 is authorized for appropriation to the Children's Bureau."

In a paper published in the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, January, 1945, page 128, Daily probably expressed the views of the Children's Bureau in advocating hospital care by specialists for all maternity cases. The number of specialists requisite is estimated at 10,000, the annual compension to vary from $2,000 to $20,000. The necessary hospitals could be built and equipped over a period of ten years at an annual expenditure of $15,000,000.

The estimated cost of providing medical and hospital care for all maternity patients would be about $250,000,000 yearly or about $100 for each birth.

The EMIC program, which reached a peak load of some 20 to 25 per cent of all deliveries, should give some idea of the amount paid by the Federal Government for medical and hospital care for these maternity patients and their babies, but it is to be doubted that this is an accurate index of the actual cost, and it is seriously questioned whether or not it would prove to be satisfactory compensation for the type of service which should be had. Under this plan the government has made payments to the individual doctors and hospitals, usually on a flat fee basis and a per diem cost plan. While the family has been relieved of financial burden and responsibility it is to be seriously doubted whether or not the quality of care has been improved.

The main theme of this paper has been to show governmental trends by documentary evidence. The Children's Bureau has been the Federal agency which has been interested in the welfare and health of children and women. The quoted evidence shows that the original concept was not that which now constitutes its major activity, namely, a "Health Agency." Its activities have changed from investigation, advising, and administration, to supervision, administration, and service. It is now concerned with women as well as infants and mothers. Under the now proposed act of 1945, all individuals under 21 years of age come under its domain. Primarily the programs have to do with health as distinguished from welfare.

If one considers the scope of the proposed act, the only portion of our population not included within its provisions would seem to be that relatively small proportion of males who are over 21 years of age.

Health is not acquired in or limited to any one sex or age period or to any physiologic or anatomic state. Health is something that is positive and not merely negative. As applied to individuals and communities it is the result of carefully integrated comprehensive knowledge intelligently applied.

The application begins with the individual and extends up through the family and the community to include progressively larger units of government, and with present trends no one nation can be a law unto itself. There must be one unified health agency based upon local units of varying size and extending upward to one Federal health agency. At present there would seem to be two major Federal health agencies developing: one in the Children's Bureau and the other in the United States Public Health Service, with budgets amounting to millions of dollars yearly. There are also other Federal departments which have major health activities which are related to their principal functions. The growth of these Federal health agencies with increase in personnel and appropriations has been rapid and phenomenal, and one wonders how much of the national income can be absorbed by the Federal government without seriously curtailing the amount of money available to the local communities for taxation to support their health and educational activities. How much of the national income can be diverted to Washington to be redistributed to the various communities from which it came without eventually limiting this taxing ability of the States and local communities? These are matters for the economists to discuss and perhaps decide, but we as citizens and doctors are seriously concerned about these trends in the functions of Federal bureaus and departments.

There is much in the reports to indicate that the Children's Bureau assumes credit for progress in the field of maternity and infancy and, while without doubt the Bureau has contributed much, it must be remembered that medical sciences have progressed independently and that the advice of medical experts familiar with these advances have been gratuitously available to the Bureau.

These experts in their various fields have been the leaders, and the Bureau has been the medium. The point which should be stressed is that these men of science have been the product of the American system of medical education, investigation, and practice. America has now advanced to world leadership in the medical sciences, and the major issue is flatly before us and the citizens of our country. Should present governmental trends be permitted to change seriously, by legislative act, an educational, research, and service system of medical care which has stood the test of time, of war, of pestilence, and of peace, and which is still progressing on all fronts? Should not the present program be evolved and not be submitted to revolutionary hothouse development? Should it not be developed upon a basis fundamental to our form of democracy and in accord with the dignity of the individual citizen and of a worthy profession?

Let it not be forgotten that the quality of medical service depends upon the quality as well as the quantity of those who render it. The medical profession must be progressively maintained both qualitatively and quantitatively.

Lastly, the rendering of high quality medical care depends not only upon personnel but also upon adequate facilities, which have never been available in all areas through no fault of the medical profession.

Let the cooperative efforts of Federal, State, and local resources provide the facilities, and private professional enterprise develop the personnel.

THE RH FACTOR IN OBSTETRICS*

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SELDOM has a medical discovery been accorded practical application as widely and intelligently as that which has followed the announcement of the Rhesus blood factor by Landsteiner and Wiener in 1940. In four years' time, not only has its implications in blood transfusion been taken into account, but a great deal has been learned concerning the various complications it imposes in the obstetric field. All this activity is in sharp contrast to the more important announcement of the A and B blood factors by Landsteiner in 1901, after which a considerable number of years elapsed before blood grouping and blood matching became well understood or widely used by the medical profession. The difference in reaction may be taken as a measure of the importance that blood transfusion and hematology in general have assumed in medical practice.

Although the Rh factor is important to all who use blood as a therapeutic agent, it is particularly in the field of obstetrics that this discovery has its greatest significance, because not only is the obstetrician concerned with untoward transfusion reactions, but also he must take into account the fact that the transfusion of an Rh-negative patient with Rh-positive blood, on the one hand, or the harboring in utero of an infant which has inherited Rh-positive blood characteristics from an Rh-father, on the other, may induce the production of antibodies which may and often do affect the offspring adversely. In fact, this process may seriously modify the reproductive period of as many as 15 to 18 per cent of women in the childbearing period of life.

It is well for us, therefore, to understand in so far as is possible the various elements of the problem which this characteristic of the red blood cell imposes upon us.

Historical Background

Although rapid progress has followed Landsteiner and Wiener's announcement in 1940, actually the sequence of events leading up to that enunciation occupied a considerable period of time. As long ago as 1905 Dienst noted that a remarkably high postpartum titer of agglutinins in maternal blood serum occurred when the mother's blood contained an A or B agglutinin which was capable of agglutinating the red blood corpuscles of her offspring. He believed that this resulted from an antigenic action of fetal blood cells

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†Assisted by a grant from the Columbia Foundation.

which had somehow gained access to the maternal circulation. Others, Murray in 1910, McQuarrie in 1923, Ottenberg in 1923, Gruhzit in 1924, and Allen in 1926, pondered the concept of fetal and maternal incompatibility in trying to explain eclamptic toxemia with various resulting opinions. It was not until 1938 when Darrow approached the matter from the point of view of the incidence of erythroblastosis that anything like our present hypothesis was forthcoming. She suggested that there was a fundamental difference in the chemical constituents of fetal and maternal blood of such a kind that a maternal reaction to the fetal type occurred and was followed by transmission of the resulting maternal antibodies through the placenta, bringing about agglutination of fetal cells and subsequently the syndrome known as erythroblastosis fetalis. Her hypothesis lacked confirmation.

Meanwhile, a parallel group of observations concerned primarily with transfusion reactions had stimulated a trend of thought which also lead to conclusions somewhere near the truth as we now understand it. Stetson, in 1933, reported the history of a young woman who, after five successful pregnancies, then had serious transfusion reactions during a series of blood transfusions when the husband was the donor, meanwhile tolerating the blood of brothers as donors with no reaction. He postulated that an inherited isoagglutinogen must be present in the members of the patient's own family and that the transfusion of foreign blood (husband) probably stimulated the production of agglutinins such that it caused reactions to the bloods of all persons outside her family.

Culbertson and Ratcliffe, Parr and Krischner, Goldring and Graef were others who reported transfusion reactions under circumstances which suggested that "intragroup" transfusion reactions were due to antibodies induced by transfusion or produced by a pregnancy.

It was not until 1939, however, that Levine and Stetson reported an irregular isoagglutination reaction in which a pregnant woman agglutinated 80 per cent of the blood of donors of the same blood grouping, and inferred that she had become immunized to some factors which had been inherited by the fetus from its male parent.

It became quite probable, therefore, that when atypical agglutinins were present, producing a transfusion reaction, several other factors were also true: either the patient had had previous transfusions or had been recently pregnant, or that the blood cells of the immediate family, exclusive of the husband, were the only ones which the patient's serum did not agglutinate. On the other hand, it was shown that the husband's blood was most likely to cause a severe transfusion reaction. Furthermore, the possibility had been suggested of fetal inheritance of paternal antigens, which were absent in the mother, resulting in the production of maternal antibodies of such a titer that a reaction followed transfusion from many donors.

In 1940 Landsteiner and Wiener demonstrated an agglutinogen in the blood of the Rhesus monkey. After injecting monkey blood into rabbits, the serum of the latter contained agglutinins capable of reacting with a high per-

centage of human red blood cells. They designated these agglutinogens as "the Rh factor" because it was found to be a constant characteristic of the red blood cells of the Rhesus monkey. Those human cells which were not agglutinated by the antirhesus serum were designated as Rh negative, whereas those which were agglutinated by it were called Rh positive.

Wiener and Peters, in 1940, made the first practical application of the Rh immunizing principle when they demonstrated that three Rh-negative persons having transfusion reactions following the use of homologous bloods probably had been transfused and sensitized previously with Rh-positive blood.

In the same year Levine demonstrated that a number of women who had had repeated abortions possessed blood sera in which isoagglutinins similar to the Rh factor were present. Following this lead, Levine and his co-workers investigated a number of women who had given birth to erythroblastotic infants and discovered that most of the mothers were Rh negative and, furthermore, that the incidence of Rh negativity in this group was many times that found in the general population. This led to the hypothesis that erythoblastosis fetalis is the result of the formation of Rh agglutinins on the part of the Rh-negative mother either as the result of transfusions of Rh-positive blood or the harboring of an Rh-positive fetus. In the latter instance, they postulated transmission of fetal red cells into the maternal circulation (due to an imperfect placental barrier) with the resulting formation of agglutinins which then retraversed the placenta and produced agglutination and probably hemolysis of the fetal red blood cells.

Thus has grown our present concept of the operation of the Rh factor in transfusion and in pregnancy.

Incidence of Rh Factor in the General Public

As a result of the investigations of numerous workers, the incidence of Rh positivity and Rh negativity in various parts of the world has become known. Altogether more than twelve thousand individuals have been tested, with results showing about 85 per cent to be Rh positive and about 15 per cent Rh negative. Table I, from Potter, gives the sources of this information. It has been found that there are racial differences in these characteristics.

TABLE I. RACIAL DIFFERENCES IN REACTION TO STANDARD ANTI-RH SERUM OF THE TYPE AGGLUTINATING THE CELLS OF 85 PER CENT OF WHITE PERSONS (FROM POTTER)

AUTHOR	RACE	TOTAL NUMBER OF SUBJECTS	REACTION TO ANTI-Rh SERUM			
			POSITIVE		NEGATIVE	
			NO.	%	NO.	%
Combined data	White	7,620	6,485	85.1	1,135	14.9
Landsteiner and Wiener	Negro	113	104	92.0*	9	8.0*
Levine	Negro	264	252*	95.5	12*	4.5
Landsteiner, Wiener and Matson	American Indian					
	Full blooded	120	119	99.2	1	0.8
	Mixed blooded	155	148	95.5*	7	4.5*
Levine and Wong	Chinese	150	149	99.3	1	0.7

*Figures calculated from author's percentages.

Whereas the white race is approximately 85 per cent Rh positive, the Negro is about 93 per cent, and the Indian and Chinese from 95 to 99 per cent Rh positive.

In our own experience (Table II) in analyzing 1,479 blood specimens we have found 82.4 per cent to be Rh positive, and 17.6 per cent to be Rh negative. The relationships to the other blood factors are shown.

Inheritance of the Rh-positive characteristic is of considerable importance, therefore, particularly in white populations. It has been found that it is inherited as a dominant in the Mendelian manner. Landsteiner and Weiner have found that inheritance is brought about by two allelic genes which they have represented as Rh (positive) and rh (negative). The phenotype Rh positive would embrace genotypes Rh Rh (homozygous) and Rh rh (heterozygous), while the phenotype Rh negative would include only rh rh inheritance.

II

TOTAL NUMBER OF
BLOOD SPECIMENS ANALYSED AS OF 6-30-44
PERCENTAGE DISTRIBUTION

GROUP	Rh+	Rh-
AB	30	31
A_2B		
A	41.7	40.6
A_2		
B	11.2	10.3
O	44.2	46.0

TOTAL NO: 1479
% Rh+ : 82.4
% Rh- : 17.6

II_1.

INHERITANCE OF THE Rh FACTOR
Material obtained from study of 60 Rh negative women from U.C.H. Obstetrical Department.

		FATHER	
		Rh negative 15%	Rh positive 85%
CHILD	Rh negative 40%	9=100%	15=29% ∴heterozygous♂
	Rh positive 60%	0	36=71%

The accompanying table (II_1) indicates the inheritance as disclosed by our study of sixty Rh-negative women, their husbands, and the resulting offspring. Forty per cent of the offspring were Rh negative and 60 per cent were Rh positive. Of the Rh-negative matings, 100 per cent were Rh negative, which might be expected. However, of the matings of Rh-positive husband and Rh-negative wife, 29 per cent of the offspring were Rh negative, which can only be interpreted by postulating that some of the husbands were heterozygous. The remaining 71 per cent were Rh positive, the result of homozygous parentage or the inheritance of the dominant Rh (plus) gene from a heterozygous parent.

However, the matter of Rh phenotypes does not appear to be as simple as this formula might imply, for it has been discovered that there are several groups and subgroupings of Rh-positive phenotypes, eight in all, as the accompanying table (III) from Wiener, Sonn, and Belkin will indicate, and with these as phenotypes at least twenty-one genotypes are theoretically possible. It is, therefore, obvious that there are many possible types of Rh positivity, the meaning of which in terms of transfusion and reproductive compatibility remain to be studied. Indeed, we may conclude that the full importance of the relationships of Rh-positive and Rh-negative blood characteristics must be the subject of extensive and prolonged study before any exact formula can be framed as to their ultimate significance.

TABLE III. THE RH BLOOD TYPES AND THEIR THEORETIC GENOTYPES (FROM WIENER, SONN, AND BELKIN)

	REACTIONS WITH Rh ANTISERUMS					APPROXIMATE FREQUENCY IN WHITE PERSONS (NEW YORK CITY)	THEORETICALLY POSSIBLE
PHENOTYPE	ANTI-Rh	ANTI-Rh_1	ANTI-Rh_2	ANTI-Rh′	ANTI-Rh″	%	GENOTYPES
Rh	−	−	−	−	−	12.75	rhrh
Rh_1	+	+	−	+	±	50	Rh_1Rh_1 Rh_1rh Rh_1Rh Rh_1Rh' Rh′Rh
Rh_2	+	−	+	+	+	15.5	Rh_2Rh_2 Rh_2rh Rh_2Rh Rh_2Rh'' Rh″Rh
Rh_1Rh_2	+	+	+	+	+	17	Rh_1Rh_2 Rh_1Rh'' $Rh'Rh_2$
Rh	+	−	−	+	+	2.5	RhRh Rhrh
Rh′	−	+	−	+	−	2	Rh′Rh′ Rh′rh
Rh″	−	−	+	−	+	0.25	Rh″Rh″ Rh″rh
Rh′Rh″*	−	+	+	+	+	----	Rh′Rh″

*This theoretically possible type has not yet been encountered, which is not surprising considering the extremely low value of the calculated frequency of the genotype Rh′Rh″.

Modes of Development of Antibodies in Response to Rh Antigens

The Rh substance appears to be on the surface or within the body of the erythrocytes of about 85 per cent of the general populace. It is also probably present in the cells of the liver, spleen, kidney, and salivary glands as well as in the general body fluids. This characteristic develops early in life, a matter of great importance in obstetrics; in fact, it has been demonstrated as early as the twelfth week of life. Antigenic potency fluctuates greatly as might be

suspected from the possible variations in inheritance of the different Rh subgroups. This fact may explain why some transfusions, with bloods incompatible as far as the presence or absence of the Rh factors are concerned, have been devoid of appreciable reaction. On the other hand, it may also explain why some Rh-negative women repeatedly harbor Rh-positive infants without serious reactions toward the fetus.

Rh agglutinins are not normally found in the human body and must either be transmitted passively by transfusion or be generated actively as a result of transfusion or pregnancy. The response on the part of the host depends upon the antigenic potency of the red blood cells introduced into the circulation as well as the ability of the recipient to produce immune bodies. Thus, some red blood cells are low in antigenic quality on the one hand and some individuals are latent reactors on the other. Whereas, the reverse and all gradations between may be true, giving rise to a wide variety of response.

In general, however, it may be said that the evidence thus far accumulated goes to show that the intimate relationship of mother and fetus in pregnancy provides a much more favorable background for the development of Rh antibodies than does transfusion alone.

It is of interest, therefore, to ascertain if possible how it may be that fetal red blood cells enter into the circulation of the mother and thus make this reaction possible. It has been known for many years that many women who die during pregnancy show at autopsy significant groups of placental cells and even placental villi which have been transported by the blood stream into the pulmonary vascular tree. This has been termed deportation of villi. It would be easy, therefore, to imagine that such breaking off of villus structures might be accompanied by a considerable number of fetal red blood cells. This may be one process whereby the intermixture of blood cells occurs. Another process, and one about which we have recent information, is the formation of hematomas about the tips of placental villi in the intervillous spaces of the placenta. Traut and Javert found several instances in which such hematomas contained nucleated red blood cells, suggesting the possibility that, due to degenerative changes in the syncytium of the placenta, such a fetal hemorrhage had occurred in the placentas of obviously erythroblastotic infants. We have no knowledge as to how frequently this may occur in so-called normal pregnancies. If it does occur, the difference in maternal reaction may be accounted for on the basis that the Rh characteristics may become well defined in the infant before that of the A and B factors.

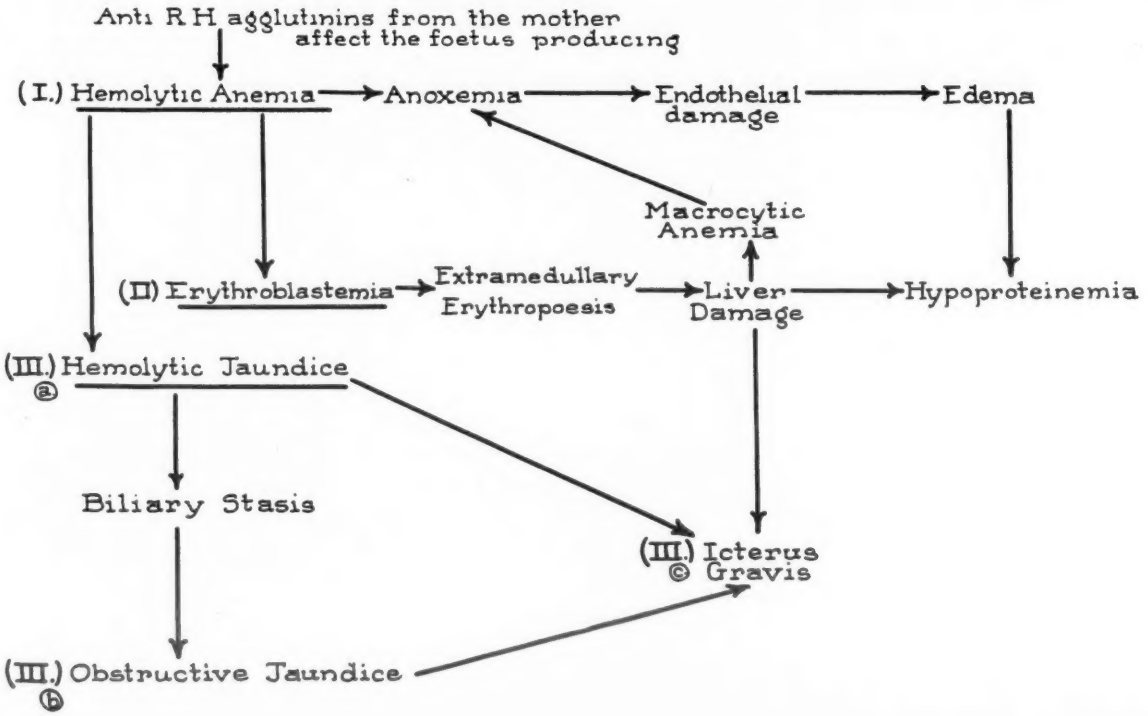
Whatever the mechanism may be for providing an intermixture of maternal fetal blood elements, experience has shown that the Rh-negative mother who carries an Rh-positive infant will frequently, and more often after the first pregnancy, develop Rh antibodies which she then may transmit to her progeny by way of the placenta.

The effect upon the fetus depends upon many factors some of which we do not fully comprehend.

TABLE IV

SUGGESTED PATHOGENESIS OF ERYTHROBLASTOSIS FOETALIS

(After Davidsohn)



Hemolytic Diseases and Erythroblastosis Fetalis

Curiously enough, the action of Rh antibodies in vitro results in agglutination, whereas, in vivo, the response is not only agglutination but the more extreme process of actual red blood cell destruction, namely hemolysis. The accompanying diagram, Table IV, after Davidsohn, may serve to explain the effect of this reaction upon the fetus. It is a pathologic speculation that there are two general types of reactions, red blood corpuscle destruction with its sequelae on the one hand, and hydrops on the other. That they may be interrelated and interdependent the diagram will show; however, one cannot accept this explanation except tentatively without more convincing evidence as to the relationship of hypoproteinemia and Rh agglutinins.

Erythroblastosis is an ill-chosen term, indicating as it does only one criterion of disease which may be common to a number of pathologic conditions of the newborn infant. It might be better to speak of hemolytic anemia of the newborn infant. Erythroblastosis must be differentiated from physiologic jaundice, prematurity, intracranial hemorrhage, hemorrhagic disease, congenital heart disease, congenital syphilis, sepsis neonatorum, familial acholuric jaundice, Winckel's disease, and hypoproteinemia. Despite this rather lengthy list of diseases similar at least in some respects to the typical case of erythroblastosis, the latter is not difficult to recognize. The jaundice due to hemolysis, the enlargement of the spleen and liver associated with its dysfunction, as well as the blood picture showing an abnormal number of the early red blood cells is pathognomonic. Occasionally, instead of icterus, one finds with the above, extensive and massive edema of the fetus, the umbilical cord, and the placenta. Indeed, icterus gravis would seem to be one mode of termination of the disease syndrome and fetal hydrops another. Thus far we seem to be unable to differentiate them etiologically and feel that they are alternate expressions of the effect of the Rh antibodies upon the tissues of the fetus.

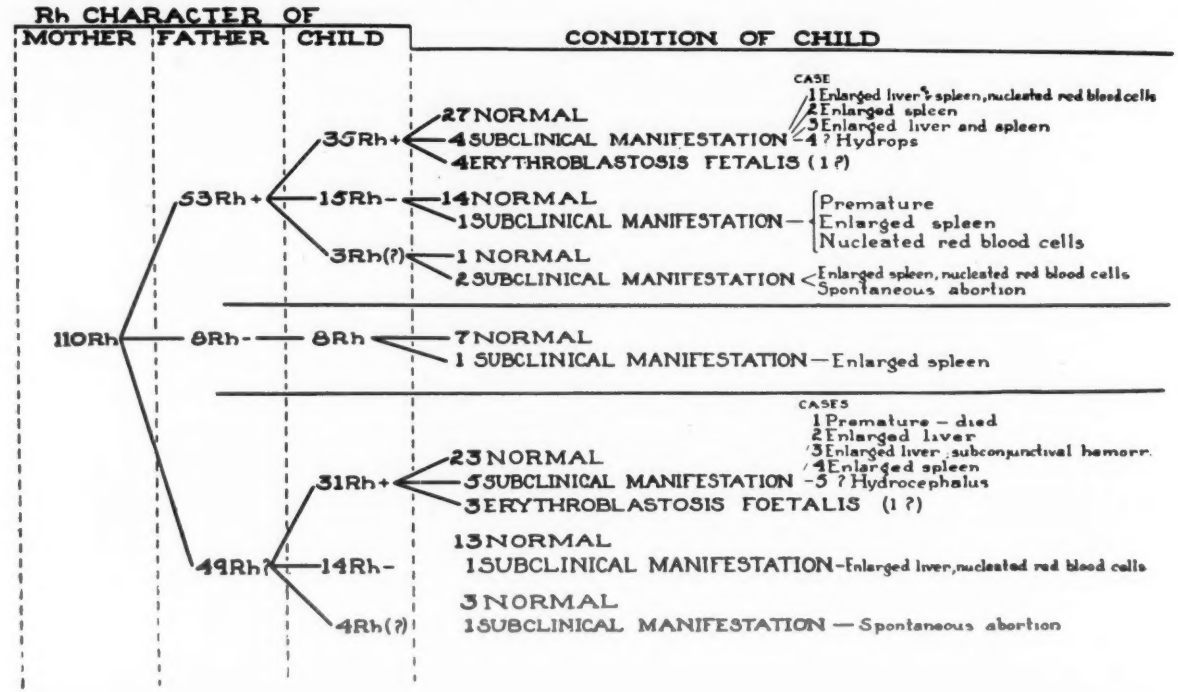
Undoubtedly, in addition to these well-defined clinical pictures there are many of lesser degree, some of them barely recognizable from the normal. It may be that the so-called physiologic jaundice of the newborn infant will eventually be found to be an expression of some blood dyscrasia, if not due to the Rh group, then to that of some other as yet unrecognized immunologic mechanism. Careful study of the subclinical varieties of the disease may be most helpful in developing our knowledge of its pathogenesis and treatment. To deny their existence is but to question biologic variation. We must expect to find all gradations.

In our experience it would seem probable that there are a number of subclinical evidences of hemolytic disease of the newborn infant, associated or not with Rh-negative inheritance, which should receive careful scrutiny in this connection. Such conditions as enlarged liver, enlarged spleen, nucleated red blood cells in excess of 5 per 100 white cells, jaundice, bleeding tendencies, anemias, hydrocephalus, and spontaneous miscarriage or abortion may or may not be related to the subject under consideration. They have seemed at times to have an increased incidence in matings involving mixed Rh factors.

TABLE V

RELATIONSHIP BETWEEN Rh NEGATIVE MOTHERS AND HEMOLYTIC DISEASE OF THE NEWBORN

MATERIAL FROM U.C.H. OBSTETRICAL DEPARTMENT — 10-13-43 — 12-31-44



Unquestionably many of the Rh-positive fetuses conceived by Rh-negative mothers do not survive to develop the recognizable features of hemolytic disease of the newborn infant. Instead, they succumb early in fetal life, in the first or second trimester. For this reason the parentage of all abortions should be carefully studied with regard to the Rhesus factor.

Relationship of Rh Negativity to the Incidence of Hemolytic Disease of the Newborn Infant (Erythroblastosis) and Subclinical Disturbances

In a group of 110 Rh-negative mothers whose bloods and that of their offspring have been studied (Table V) 66 Rh-positive infants were born. Of this group, erythroblastosis was diagnosed seven times, giving an incidence of 10.6 per cent. If our hypothesis as to the etiology of erythroblastosis is correct, one might expect a higher incidence of the disease. However, there are a number of conditions which may explain the disparity between the potential and the actual incidence. The quality of the placental barrier may be of a better sort in some pregnancies than in others; the maternal reaction to the Rh antigen may be variable; and finally, the antigen of the fetal blood cells themselves may be of different potentialities. Such possibilities make the study of the titers of Rh antibodies in the maternal blood of great importance.

In addition to the frankly erythroblastotic infants there were nine infants with definite abnormalities such as to suggest that the abnormalities may have been lesser expressions (subclinical) of the disease, thus making an incidence of abnormality for this subgroup of 14.8 per cent. If we wish to add the total incidence of abnormality for the whole group, we arrive at 24 per cent.

It is of interest to note also that there were three instances of subclinical abnormality such as we have spoken of in Rh-negative infants born to Rh-negative mothers. One of these mothers had a 4-plus anti-Rh titer throughout her pregnancy, which may have been engendered by previous pregnancies or by transfusion. The other two mothers may have been sensitized in a similar manner, but, unfortunately, we do not have the data which would enable us to make a definite statement.

Relationship of Anti-Rh Titer to the Incidence of Fetal Pathology

For some time we have been determining the titer of the Rh antibodies in our Rh-negative mothers and have expressed this as 1 plus, 2 plus, up to 4 plus. Unfortunately, the complete data upon this material and its relationship to the duration of pregnancy, together with the incidence of fetal pathology, is not yet available. However, a preliminary statement can be made at this time.

Of 21 Rh-negative women showing definite anti-Rh titers ante partum, the children of nine of them (43 per cent) showed some abnormality, four of which were frankly erythroblastotic, one was questionably so, and four showed subclinical manifestations such as prematurity, enlarged spleen, nucleated red blood cells, enlarged liver, and hydrocephalus.

There was an interesting group of 8 Rh-negative mothers who showed anti-Rh titers post partum only. In the offspring of these, two, or 25 per cent, had erythroblastosis and two more were questionable erythroblastotics. A high

incidence of abnormality, indeed. One cannot but wonder why the titer appeared only after delivery. Did the fetus so effectively absorb the antibodies as to make antepartum demonstration of them in the maternal blood impossible? Or did fetal blood become more available to the maternal circulation during the process of parturition? At this stage we can only speculate as to the real cause.

On the other hand, 37 Rh-negative mothers, showing no appreciable anti-Rh titer either during pregnancy or afterwards, produced infants on five occasions which had some of the subclinical manifestations. There were no instances of frank erythroblastosis in this group.

The study of titers is, therefore, only suggestive in the sense that the intensity and the timing of the maternal reaction may bear some relation to the effect of the antibodies upon her offspring.

Observations Upon Rh-Positive Mothers Married to Rh-Negative Husbands

The frequency of the relationship of Rh-negative fathers and Rh-positive mothers is one of the unknowns in this field and will remain so until it is possible to determine the pedigree of *all* marital relationships. We do know, however, that this relationship may be associated with fetal inheritance, bringing into play agglutinogens to which the mothers react in a manner deleterious to the offspring. We have encountered one instance of erythroblastosis and five instances of subclinical abnormality, one of the latter being a case of Kern icterus.

Treatment of Newborn Infants Having Hemolytic Disease

The first requirement is to be forewarned. To accomplish this we may sometime decide to pedigree all bloods of married couples. Certainly this is as important to the welfare of society as the legally required Wassermann reaction for syphilis. At least we can say that all women who have had transfusion reactions and all secundigravida and all women having had repeated abortions or fetal anomalies of a suggestive nature should be investigated, and, if found Rh negative, then their husbands should be accorded the same study.

As many of the offspring who succumb to hemolytic disease do so during the last few weeks of pregnancy, it has been suggested that pregnancies might be terminated before the end of the tenth lunar month. It is doubtful whether this would be of any avail as more infants die neonatally of this disease than are stillborn and, in addition, one would have the added handicap of prematurity with which to cope.

Certainly the avoidance of any means of analgesia or anesthesia which is associated with a decreased oxygen-carrying capacity on the part of the maternal blood should be practiced during labor or delivery.

It may be, however, that when we learn more about the titers developed by mothers, a high level which begins to drop may be an indication of increased rapidity of absorption of the antibodies by the fetus and that interruption of pregnancy at that time would result in a reduced degree of damage to the infant.

At present, the most important feature in the treatment of hemolytic disease of the newborn infant seems to consist in prompt transfusion of the infant with Rh-negative blood from some other donor than the mother. This should be repeated in all probability on several occasions. As a rule, a red blood count of 3,000,000 or less is indication for transfusion, and if 5 per cent or more of the cells are nucleated, then the urgency is increased. If the red blood count be as low as 2,000,000, the chance of survival of the infant is small and all haste should be used to transfuse. Red blood counts done on cord blood as soon as the infant is born should be routine procedure on all infants of Rh-negative mothers. Such a precaution provides the earliest means of recognition of a hemolytic anemia which may have been active in utero. Thereafter, the counts should be repeated at six-hour intervals. Other procedures, such as the administration of vitamin K to check a bleeding tendency, while doing no harm, probably serve no useful purpose because the liver damage causing the bleeding tendency has already occurred and usually the infant does not lack vitamin K. At any rate, vitamin K frequently fails to alleviate the bleeding tendency.

Oxygen therapy has proved to be of some assistance, particularly in the icteric and anemic groups of infants, especially if the red blood count be markedly reduced. The hydropic type of fetus offers the greatest challenge because of the marked hypoproteinemia as well as anemia. The mortality in this group is so high that only the most prompt exercise of the above measures offer any hope for survival.

The Need for Clarification of the Clinical Diagnosis of Erythroblastosis

The diagnosis of the lesser degrees of erythroblastosis offers considerable difficulty because they may closely resemble physiologic jaundice, jaundice due to birth injuries, septicemia, and a variety of anemias of the newborn infant. Clarification will come only as a result of the close cooperation between obstetrician, pediatrician, hematologist, and pathologist. This is all the more important because it is in this group that the greatest hope of salvage lies. The recognition of the possibility of isoimmunization in antenatal obstetric patients will provide the background for prompt and special care on the part of the obstetrician. This, followed by examination of the cord blood at the time of birth, with transfusion if severe anemia or nucleated red blood cells be found in excess of 5 per cent, will add to the life expectancy of the infant. If, in addition, liver or spleen enlargement or icterus be present, the diagnosis becomes clearer and the need for prompt measures is definitely indicated. When survival of the infant is not achieved, careful autopsy studies are of the greatest importance in establishing the cause of death, and in clarifying the clinical impressions which have proceeded death.

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THE SURGICAL CORRECTION OF CONGENITAL APLASIA OF THE VAGINA

An Evaluation of Operative Procedures, End Result, and Functional Activity of the Transplanted Epithelium

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ALTHOUGH congenital absence of the vagina has been recognized since earliest antiquity, its surgical correction began only a little over a century ago. Since the first reported attempt at surgical correction by Dupuytren[1] in 1817, there have been many hectic years of trial and error, of weighing the psychological evils of the anomaly against the risks of operation. Today, fortunately, all this has changed. There no longer appears to be any valid reason why girls with congenital aplasia of the vagina should not receive the benefit of modern surgical correction, and at a sufficiently early age to minimize psychological trauma. For these young women there are today satisfactory methods of treatment, but this was not always so. Indeed, the cycle through which their wheel of fortune has revolved represents a small, but interesting phase in gynecologic history. Steinmetz[2] presented an interesting historical review of the subject in 1940.

The incidence of vaginal aplasia is not definitely known, but Engstadt considers one in five thousand births a fair figure. Probably the condition is more common than was formerly believed because some afflicted individuals fail to seek treatment and many treated cases remain unreported. While the condition must have been recognized since earliest times, Burrage[2] states that the first reported case was described by Realdo Columbus in 1752. By 1895, however, Neugebauer had knowledge of one thousand collected cases.

The condition represents an embryonal or developmental defect and may reveal itself as a partial or complete absence of the vagina. Since the genital and urinary organs have a close embryonic origin, developmental anomalies of adjacent urinary organs may also be encountered. This is an important point to remember since a pelvic mass found in connection with aplasia of the vagina may mean a pelvic kidney. One of our patients had only one kidney (Fig. 1). Counseller and Sluder, Jr.,[3] investigated 15 of their patients urologically and found only 6 had normal kidneys. Of the remaining 9, the left kidney was congenitally absent in 6. Two had ectopic pelvic left kidneys and one had a duplication of the left ureter.

Earliest treatment probably included pressure makeshifts of one sort or another. Their use is but dimly recorded and leaves much to the imagination. First attempts at

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surgical treatment remain sketchy, but, in 1904, James F. Baldwin[4] described a contemplated operation whereby he hoped to use a loop of terminal ileum or sigmoid colon, carrying it down through a newly dissected channel between the bladder and rectum. Baldwin believed there would be sufficient mesentery to permit such mobilization of the bowel (Fig. 2). He did not, however, have an opportunity to try this technique until 1907. By 1910, he had successfully operated on four patients by this method. Meantime, Mueller[5] and Mori[6] each reported a successful case operated by Baldwin's technique, making a total of six cases without mortality.

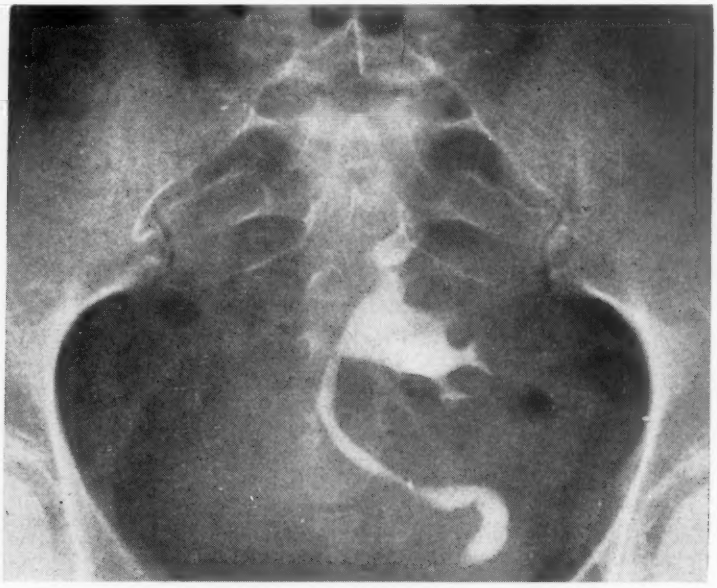

Fig. 1.—Single kidney located in the pelvis, as found in our case No. 534092, reveals type of associated urinary tract anomaly that must be looked for.

Competition now developed between the exponents of the Baldwin technique and the operation devised by Schubert[7] wherein the lower rectum, except for the anal orifice and sphincter, was moved forward to function as a vagina (Fig. 3). The continuity of the alimentary tract was restored by pulling down and attaching the lower cut end of the sigmoid to the anal ring. This method was popular among European gynecologists and was considered less formidable and, therefore, less hazardous than the procedure advocated by Baldwin. By 1927, Schubert was able to report a mortality of only 3.2 per cent as compared with a 17 per cent mortality rate for the Baldwin operation. The fact that Wagner[2] reported a case of vaginal aplasia treated by Schubert's method where the patient later successfully gave birth to three children further served to boost the popularity of this operation. Doubtless both of these techniques would have increased in popularity had not the associated mortality and morbidity continued to serve as a sobering influence. These same drawbacks, however, served to stimulate development of other, less hazardous, plastic procedures, and during the next quarter century there appeared numerous new operative techniques. Most of these called for dissection of a channel between the bladder and bowel plus the lining of this channel with skin derived either from the labia (Graves,[8] Davis and Cron,[9] Falls[10]) or from the thigh (Frank and Geist,[11] Grad,[12] Dannreuther,[13] Flynn and Duckett[14]) (Figs. 4, 5, and 6). Many variations in all of the basic techniques resulted as time went on. This plastic era was characterized by reduced mortality if not by brilliance and usefulness of the results obtained. We cannot speak for others, but, in

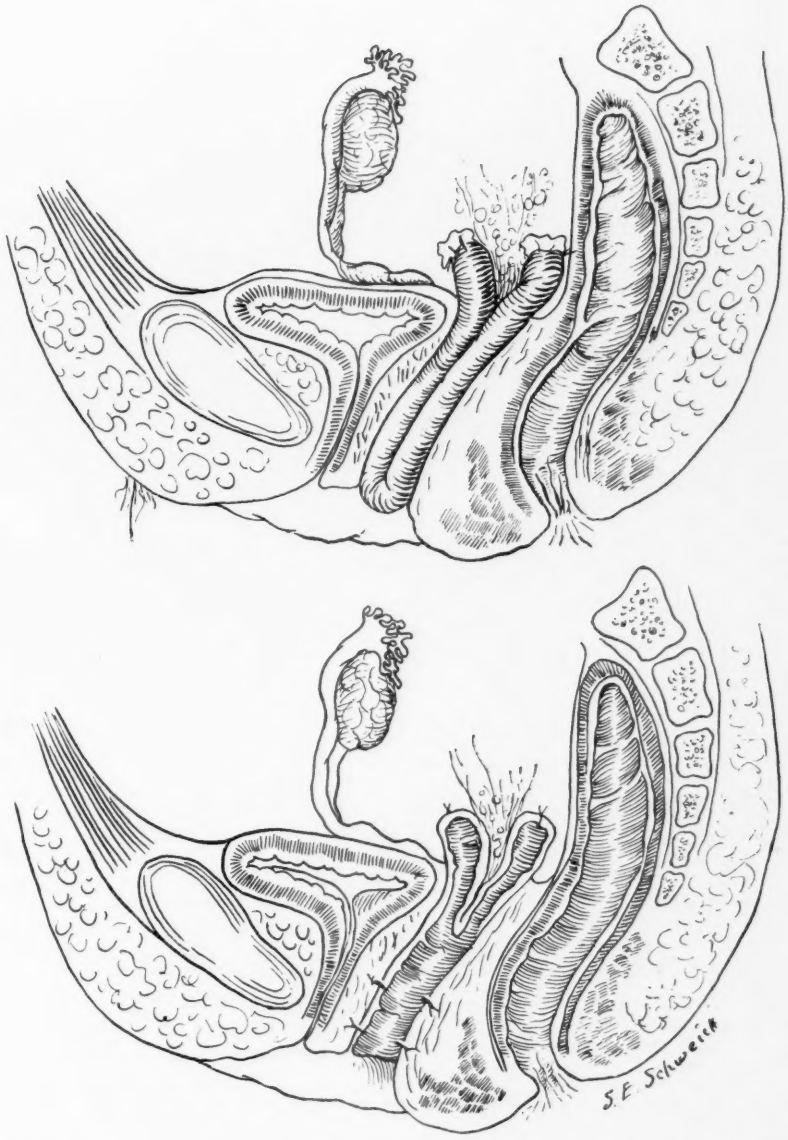

Fig. 2.—Baldwin operation: illustrating use of terminal ilium in formation of new vagina.

our hands, the results following these cumbersome "satchel-handle" tube grafts or the use of labial skin were not satisfactory. The plastic procedures nevertheless represented a forward step in the evolution of a safer and more acceptable method of treatment.

It had long been known that pressure, properly directed and over a sufficient length of time, ultimately produced a vaginal channel of some depth. Frank[15] re-emphasized this principle in 1938 (Fig. 7). Simplification of surgical treatment, however, was given a real boost when, in 1935, Wells[16] reported the use of petrolatum-gauze packing in a dissected vaginal channel. The vaginal gauze was replaced every forty-eight hours and, at the end of one month, he noted that the mucous membrane had grown up into the channel for a distance of 1 inch. Two subsequent deeper dissections, each followed by packing, ultimately led to the formation of a 4-inch epithelium-lined vaginal tube. In 1938, Wharton[17]

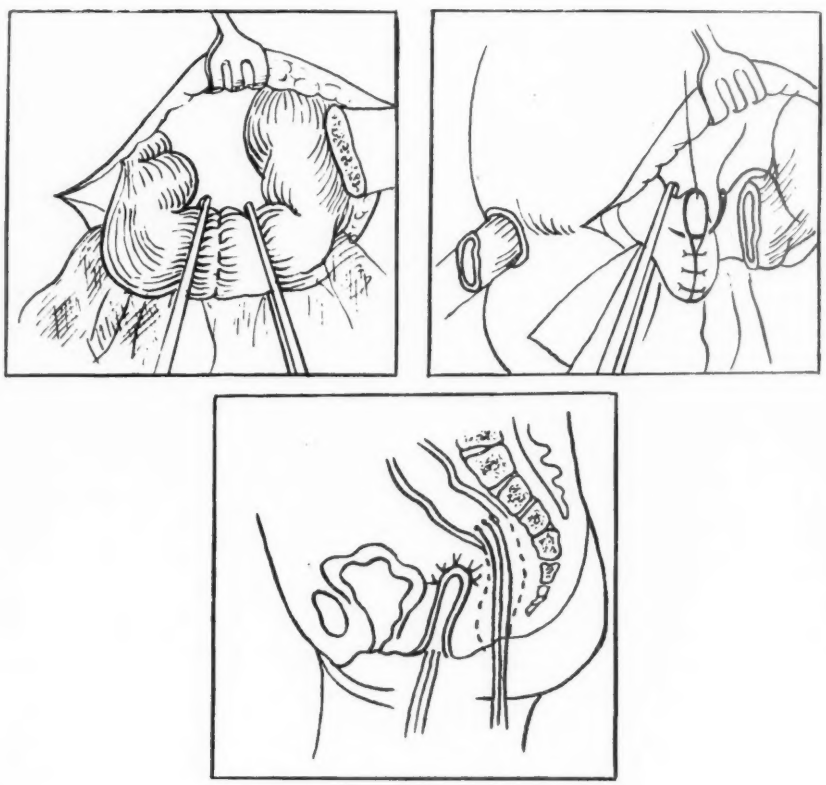

Fig. 3.—Schubert type operation.

emphasized the remarkable proliferative power of the vaginal or vestibular mucous membrane and outlined his method of treatment. This consisted of the usual dissection between the bladder and rectum and the maintenance of patency for at least three months by the use of a wax-filled condom or balsa wood mold. Wharton described four cases successfully treated by this method. In 1940, he reported twelve so treated by seven different surgeons with successful outcome in each case. He also emphasized the importance of postoperative care.

Kerschner and Wagner[2] used Thiersch grafts sutured over a rubber sponge and placed into the newly dissected channel. On removing the sponge, eight to ten days later, the grafts were seen to have taken. Dilators were subsequently used to prevent contraction. Barrows[18] favored this procedure because there was no serious morbidity. No scars

of any significance remained and there was no prolonged hospitalization. Furthermore, the new lining closely resembled normal vaginal mucous membrane. Barrows described two patients so treated and stated that in thirty-two collected cases poor results occurred only twice.

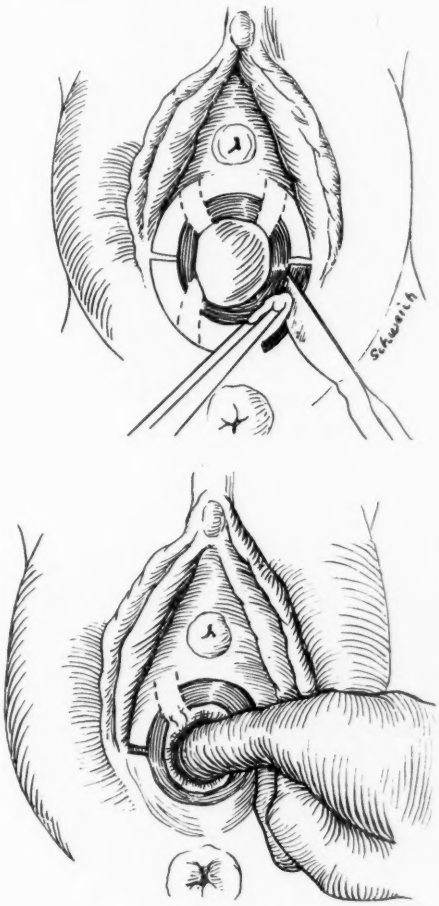

Fig. 4.

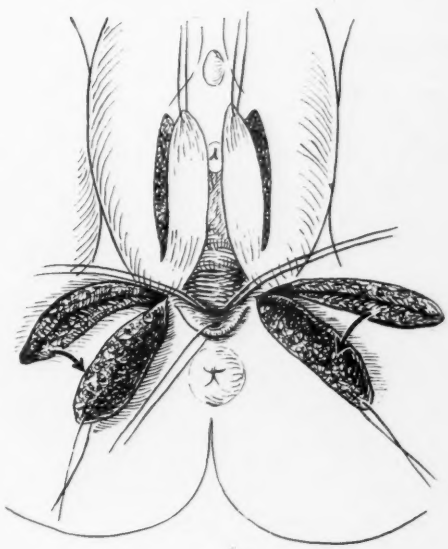

Fig. 5.

Fig. 4.—For lining newly dissected channel, Falls used mucous membrane flaps obtained from the vestibule.

Fig. 5.—Illustrating use of skin flaps for lining newly dissected vaginal channel as described by Douglass in 1934.

In July, 1938, McIndoe and Bannister[19] reported using a thin skin graft over a vulcanized mold inserted into the newly dissected vaginal channel with complete take of the graft. Ultimately, a normal looking vagina was produced. An obturator was left in for three months in order to prevent contraction. Counseller[20] popularized this procedure in this country and in 1938 reported on his experience by this method. In 1944 Counseller and Sluder, Jr., recorded thirty-five cases treated by this method. Reports of cases similarly treated are appearing with more and more frequency and with generally favorable comment as to the results obtained. We, too, have used the split thickness skin graft method with good results.

Treatment of congenital aplasia of the vagina has now progressed to the stage where it no longer is necessary to deny treatment to any girl with this

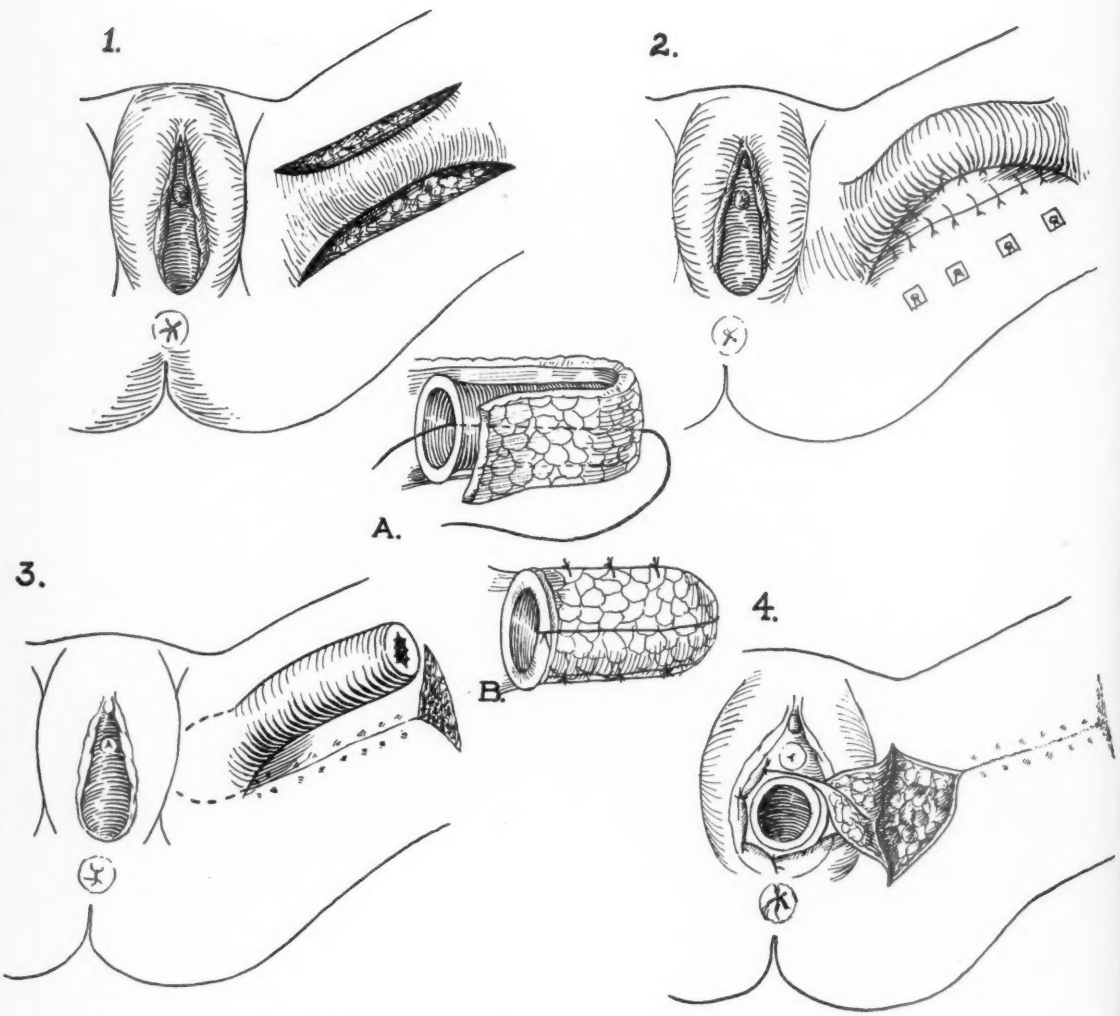

Fig. 6.—Illustrating the Frank-Geist "satchel-handle" type tube graft operation. Extensive long-drawn-out plastic procedures of this type are no longer necessary or desirable.

condition, nor is it necessary to wait until the young woman has had an offer of marriage before proceeding with treatment. Indeed, when correction is made dependent on an offer of marriage, it emphasizes the abnormality and increases the psychological drawbacks which commonly go with anomalous congenital development of any kind.

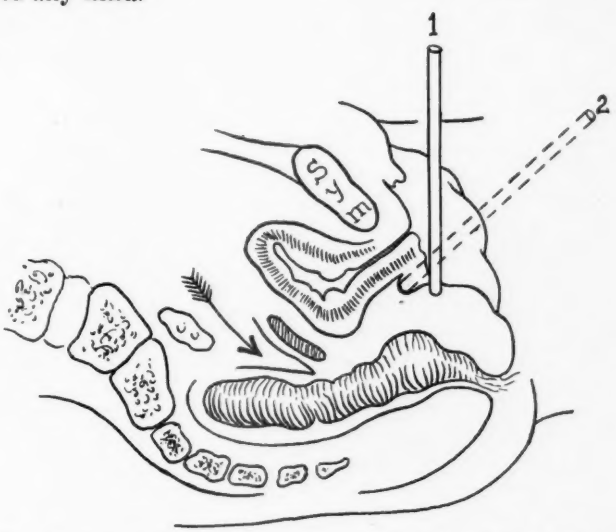

Fig. 7.—Nonsurgical pressure correction of congenital vaginal aplasia as described by Frank in 1938.

Our interest in congenital aplasia has been twofold. Like many others we wished to know the most satisfactory and the simplest method of correction. To this end we reviewed the literature and decided, some years ago, on the basis of this review as well as on the past experience of the senior author, that, while no one method might be universally acceptable, all evidence, including our own experience, pointed with preference to one of two procedures. Either the formation of a channel between bladder and bowel and the continued use of an obturator until epithelization had taken place by ingrowth from the vestibular epithelium, or else dissection and the use of a split-thickness skin graft-covered obturator such as advocated by Kerschner and Wagner, Barrows, McIndoe and Bannister, Counseller, and others. During the past decade we have used both methods and, in this report, present the results in our series of seventeen cases (See Table I).

Our second interest in this problem was to learn something of the behavior of the transplanted epithelium in those cases where a skin graft was used in lining the dissected channel.

Before listing our results and data, however, we present in brief outline the steps followed in the correction of our cases.

1. Careful history and physical examination, including intravenous pyelograms and such other studies as may be desirable in order to rule out associated anomalies of the genitourinary tract.
2. Customary preoperative preparation: enema, catheterization, etc.
3. General anesthesia.

TABLE I

SERIES NO.	CASE NO.	GENERATIVE ORGANS PRESENT			TYPE OF OPERATION		RESULTS	COMMENTS
		VAGINA	UTERUS	OVARIES	DISSECTION. OBTURATOR ONLY	DISSECTION. SKIN GRAFT ON OBTURATOR		
1	426577	Absent	Absent	Present		Yes	Unsatisfactory	Slough of graft severe reaction due to plastic obturator. Fistula for few days. Now married. Tender scarred vagina
2	476743	Deep vestibular pouch	Absent	Present		Yes	Satisfactory	
3	486286	Absent	Absent	Present		Yes	Satisfactory	
4	497804	Absent	Absent	Present		Yes	Satisfactory	
5	474074	Shallow vestibular pouch	Present	Present		Yes	Satisfactory	Slight scarring near cervix
6	510921	Lower half absent, upper half of a hematocolpos	Present	Present	Yes		Satisfactory	
7	511392	Absent	Absent	Present		Yes	Satisfactory	Vagina not full length
8	529316	Slight vestibular pouch	Absent	Present	Yes		Unsatisfactory	Required dilatation. Ultimate result good
9	529599	Slight vestibular pouch	Absent	Present			Satisfactory	
10	537113	Absent	Absent	Present	Yes		Satisfactory	
11	545507	Tiny channel 1/8" diameter	Present	Present	Yes		Unsatisfactory	Patient was pseudohermaphrodite reported as Case 12
12	545507	Reoperation —same patient as No. 11			Yes		Satisfactory	
13	534092	Absent	Absent	Present		Yes	Satisfactory	Only one kidney located in pelvis
14	312924	Absent	Absent	Present		Yes	Satisfactory	
15	562787	Slight vestibular pouch	Present	Present		Yes	Unsatisfactory	Required dilatation. Ultimate result good
16	568002	Pouch produced by first marriage	Absent	Present		Yes	Satisfactory	
17	566545	Pouch and tiny channel to cervix	Present	Present	Yes		Satisfactory	Good result

4. If a skin graft is to be used, it may be obtained at this time. We prefer a split thickness graft, 12 to 15 thousandths of an inch thick, taken either from the abdomen or the thigh. The use of a Padgett or other type dermatome and a good sticky mastic greatly facilitates this part of the operation. The graft obtained should be adequate to permit covering the obturator.

5. Dress wound site from which graft was taken.

6. Patient is now placed in lithotomy position, and genitalia carefully reinspected.

7. A transverse incision is now made in the vestibular mucosa about midway between the external urinary meatus and the posterior vaginal fourchette.

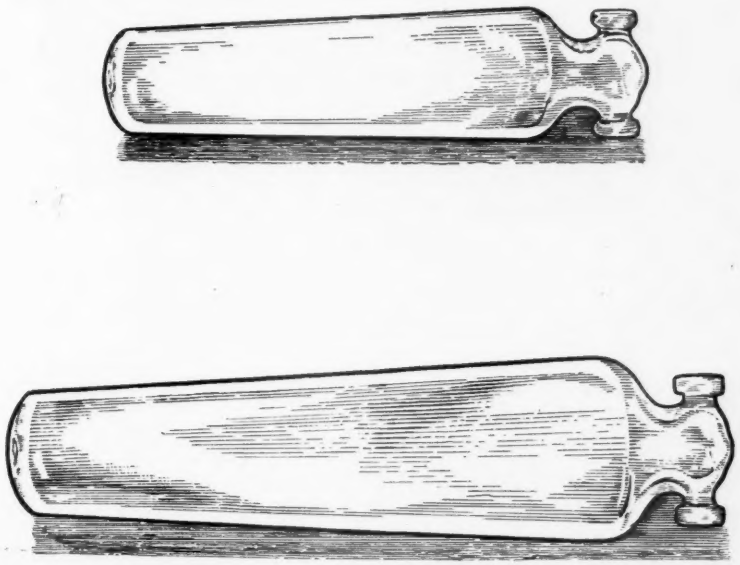

Fig. 8.—Obturators made of glass (nonbreakable when possible) and in several sizes are highly desirable in the treatment of vaginal aplasia.

8. The dissection is carried up—blunt dissection preferred—between the rectum and bladder. Once the cleavage line is found, dissection may be accomplished without difficulty and carried up the cervix, if present, or else to the peritoneum.

9. Gross bleeding is controlled by ligature and pack. If the pack is left in while the graft is being placed on the obturator, the oozing may be reduced.

10. Pack is now removed from the dissected channel and the graft-covered obturator inserted into the dissected channel where it is held in place by a perineal pad and T binder.

11. Place an indwelling catheter in the bladder which may be removed when the obturator is taken out on the seventh to tenth postoperative day.

12. Postoperative care involves no special problems except that it is well to limit solid food intake during the first few days.

13. On the seventh to the tenth day the obturator is gently removed and the newly formed epithelium-lined vaginal channel carefully inspected and irrigated with warm saline. This is easily accomplished since it is possible to insert a bivalve speculum and look over the new-formed channel without discomfort to the patient.

14. The obturator, after it has been cleaned and covered with a lubricant, is now reinserted. The patient may be up and about and is taught to remove the obturator (while in bed so that she does not drop and break it) before defecating and before voiding. Reinsertion is carried out in bed so the chance of breaking is minimized. In the postwar period obturators should be made of nonbreakable glass or plastic (Fig. 8).

15. The patient is discharged on the tenth or twelfth postoperative day, or whenever convenient, but should wear the obturator regularly until re-examined, usually in four to six weeks. Further use of the obturator after this period of time will depend on the findings at subsequent examinations. As a rule, however, when the obturator is discontinued, the patient should be cautioned to wear it at night until she is able to determine whether its nonuse during the day leads to increased difficulty in reinsertion. If this be the case, continued use of the obturator both day and night is warranted.

16. In patients with underdeveloped secondary sex characteristics the use of estrogen therapy may be helpful during the postoperative period as a means of stimulating epithelial growth.

17. The taking of a skin graft is obviously omitted in those cases where only dissection and the use of an obturator are planned. This procedure is not difficult if care be taken in finding the proper line of cleavage between bladder and bowel.

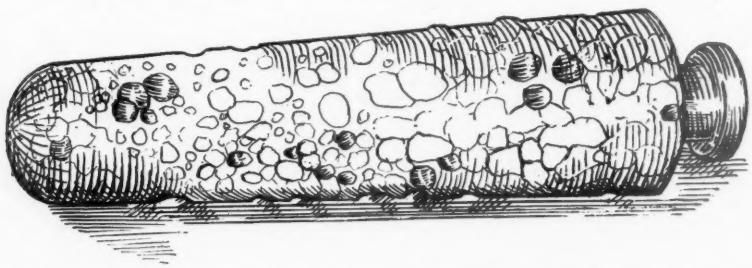

Fig. 9.—Plastic obturator once used by us. Note marked irregularity of the once smooth surface due most likely to some chemical reaction between mastic used to hold skin graft in place and plastic material in obturator. Complete destruction of skin graft occurred in this case.

In one of our early cases a plastic obturator was used (Fig. 9). As a result of some destructive chemical reaction, the entire graft was destroyed and the obturator, which had been perfectly smooth prior to use, was badly pockmarked. The tissue necrosis was so severe that the patient developed a vesicovaginal fistula which, fortunately, underwent spontaneous healing after a few days. After many months of wearing a glass obturator, this patient finally presented a completely epithelized channel, but there was not the pliability or softness that one sees in a completely successful result. The patient has since married and has a usable, though somewhat tender, vaginal tube. In this case, and in cases reported by Wells and Wharton, it is clear that the vestibular epithelium shows marked proliferative propensities, sufficiently so to permit epithelization of the dissected channel.

In order to compare the two procedures, we used the Wharton technique of dissection and the insertion of an obturator without skin graft in six of our seventeen cases. Table I shows a comparison of end results. Our standard for a successful result was an epithelized, soft, pliable vaginal tube showing no unusual or excessive amounts of scar tissue or contraction after a reasonable convalescent period (three months). While our experience is not extensive (17 cases), we feel that the use of a skin graft is definitely superior and, unless further experience and complied evidence warrants, we shall give preference to this combined procedure in those patients reporting for treatment in the future. We recognize, however, that in some instances, especially where there

is only partial absence of the vagina, dissection and the use of an obturator may be an entirely adequate, and indeed, may even be more desirable than the combined method.

While choice of operation is important, the actual behavior of the epithelium in the new-formed vagina is also of interest. In February, 1942, we had an opportunity to observe one of our grafted patients (No. 474074) one year after operation, throughout a complete menstrual cycle. Vaginal smears

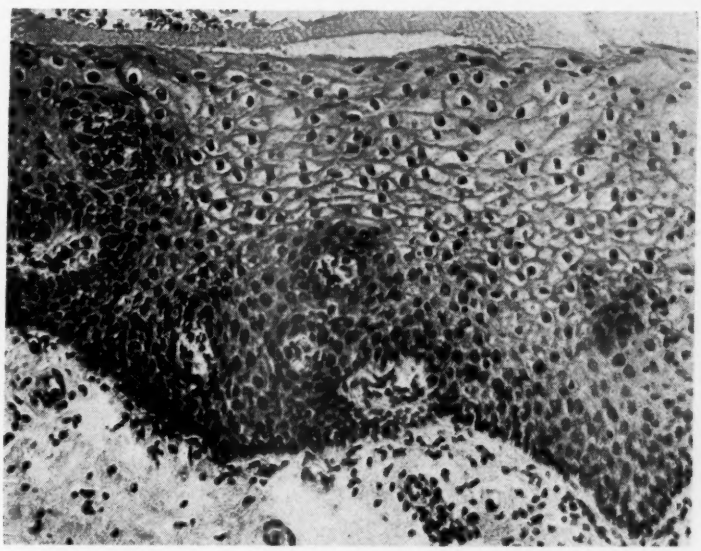

Fig. 10.—Vaginal biopsy taken on twelfth day of cycle (×260). Note typical mucous membrane appearance. Compare with Fig. 11.

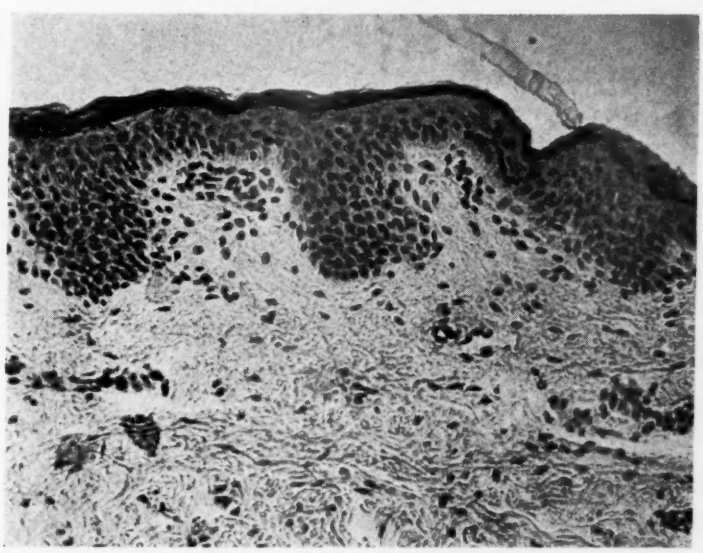

Fig. 11.—Skin biopsy taken from thigh near site from which graft for vagina was obtained. Both vaginal and skin biopsies were taken on the twelfth day of cycle (×260).

were carefully studied. In addition, several biopsies were taken from the year-old vagina and, for comparison, from near the site where the skin graft had originally been obtained. Gross inspection of the vagina at this time showed a normal-appearing, pink, mucous membrane. The surface was moist, but somewhat less rugous than is normally seen. Biopsy and histologic examination showed stratified squamous epithelium of the mucous membrane type, indistinguishable from normal vaginal mucosa (Fig. 10). The basal layer was composed of small germinative cells, above which the cells became progressively more cornified toward the surface. No keratin was present. The submucosal tissue was fibromuscular without the accessory skin structures. Daily vaginal smears stained by the Shorr technique revealed cells which could not be differentiated from those of normal vaginal epithelium. There was a gradual increase in cornification and a decrease in the number of leucocytes until the twelfth day of the cycle, when there was a complete leucopenia at the peak of cornification. On the following day the leucocytes suddenly reappeared in large numbers, and during the remainder of the cycle the smears all contained leucocytes and some folded and fragmented epithelial cells. This cycle of events is exactly the same as that which occurs in the vagina of normal menstruating women and which has been utilized in the study of ovarian function. Smears stained for glycogen by the iodine vapor method of Mack[21] showed normal amounts of glycogen to be present. There was a gradual increase in the glycogen content until the peak of estrogen stimulation on about the twelfth day of the cycle, after which it diminished. Vaginal biopsies taken on the twelfth day of the cycle and stained by the Best carmine technique showed glycogen to be present in the outer cell layer. For purposes of comparison, sections of skin were taken from near the site where the graft had been obtained. Both biopsies were taken on the twelfth day of the cycle. Histologic examination revealed normal skin with glands, hair follicles, and surface keratin layer (Fig. 11). Glycogen could not be demonstrated in the skin biopsy. Later, a total of 18 mg. of stilbestrol in oil was applied over a period of six days to a small area on the thigh, but microscopic examination of tissue taken from this site at the completion of the treatment showed no change either in cell type or in thickness of the epithelial layer. Glycogen could not be demonstrated in the biopsies from this area by the Best carmine technique.

The normal vagina, with the exception of the lowermost portion, probably represents an invasion of urogenital sinus epithelium and, despite the resemblance of vaginal epithelium to other stratified squamous epithelium, its physiology is unique. The generative tract is the only place where the control of glycogen deposition is, at least in part, an important function of the estrogenic hormone. The normal skin from the thigh transplanted into the artificially produced vaginal channel appears to assume the functions of normal vaginal mucous membrane. In the case here reported, and in the case reported by Whitacre and Wang[22] the skin lining the new tract appears to acquire the histologic, as well as the physiologic, characteristics of normal vaginal mucous membrane. Replacement by ingrowth of vestibular epithelium cannot be en-

tirely ruled out but this appears unlikely since the graft took completely and no evidence of tissue loss could be demonstrated on subsequent examinations.

As further confirmation in proving the persistence and functional activity of transplanted skin, we hoped for an opportunity to correct this anomaly in a Negro girl. It was felt that if the black pigment in the skin taken from the thigh or abdominal wall remained after being grafted into the new-formed vaginal channel and functioned as vaginal epithelium, this additional evidence would permit the concession that, under certain circumstances, transplanted skin may undergo physiologic and environmental response to a degree previously considered unlikely. It is improbable that a reversal of this situation would have any practical application but it would be of interest to know how well vaginal mucosa might function as a substitute for normal skin.

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HYPERTROPHY OF THE UTERUS*

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ENLARGEMENTS of the uterus other than those caused by tumorous growths have heretofore been designated by various terms according to the etiological and pathologic factors concerned. "Hypertrophy of the uterus" is an all-inclusive descriptive term which serves to group these various enlargements into a much needed clinical entity.

Hypertrophy of the uterus is characterized by morbid enlargement or overgrowth, particularly of the body of the uterus. It presents a pathologic complex which continues to cause much confusion among gynecologic pathologists as well as gynecologists. Nonetheless, it may well be considered as an entity, despite the various etiological factors involved and the protean picture presented.

In cases of hypertrophy the uterus is symmetrically enlarged† and heavy, or the plump, firm, ovoid corpus alone may be the chief site of change. The uterine walls are thickened, often to 3 cm. or more, the cavity enlarged beyond its usual capacity. The cut surface of the uterine wall tends to be firm and rigid, the texture tough and striated, in a measure justifying the term "fibrotic," a favorite designation which has been criticized as elusive and unwarranted except as a pathologic rarity. The blood vessels may be numerous and prominent, notably the veins, which frequently are enlarged or are seen with the naked eye as tufted nodules simulating those of adenomyosis.

The endometrium varies greatly, depending on the etiological factors concerned. It may be entirely normal or may be thickened or even polypoid in case there is hormonal imbalance or obstructed uterine drainage.

Associated with the changes in the uterine corpus, numerous and varied changes occur in the cervix, in Mackenrodt's ligaments, in the ovaries, and in the other pelvic tissues, dependent upon the etiology of the hypertrophy and the severity and duration of the process. Changes in the ovaries are naturally reflected in the uterus in so far as hormonal function is disturbed.

Classification of the etiology and pathologic histology of hypertrophy of the uterus has been difficult and unsatisfactorily, in part owing to attempts to limit the number of etiological factors believed to contribute to this pathologic complex; also because the role played by endocrine disturbances, entirely unrecognized in earlier years, is still an undetermined although very important factor. Years of floundering eventuated, some years ago, in rather wide accept-

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†Anatomic descriptions of the uterus invariably omit mention of the thickness of the healthy multiparous uterine wall, which normally measures approximately 2 cm. in the region of the greatest diameter of the uterine corpus. This basic measurement is important in evaluation of the pathologic changes to be considered in the subject under discussion.

ance of certain entities among these benign enlargements of the uterus: the old term "fibrosis uteri" became replaced by "chronic subinvolution," "true chronic metritis," and "diffuse hypertrophy of the uterus." Then, in more recent times, with recognition of the dominating influence of the hormones, the entire subject became more confused; it is currently accepted that endocrine changes account for most cases of *diffuse* hypertrophy of the uterus and also play some part in the other hypertrophies.

As a matter of fact, numerous etiological factors are concerned with hypertrophy of the uterus, just as many factors may be responsible for enlargement of any other viscus, such as the kidney, or any other unit of the human anatomy, such as the leg. In evaluating the etiology and pathology, specific local factors of influence must not be overlooked. These include menstruation and pregnancy and the hormonal changes associated therewith, also the normal and abnormal ovarian and related incretory activities at other times.

Normal puerperal involution was first described by Szasz-Schwarz.[1] In the process of involution after childbirth, with gradual degeneration of the hypertrophic blood vessels much elastic tissue always persists in the parous uterus. There are circular or crescentic collars of elastic tissue around the arteries of the inner zone of the uterine wall, thick vessels largely due to elastic tissue in all layers of the vessel walls in the middle zone, and increased subperitoneal and vascular elastic tissue in the outer zone of the uterus, where the veins are also thick walled, elastic tissue in great preponderance. This process is diagnostic of a previous pregnancy, never appears in the nulliparous uterus, and increases with each succeeding pregnancy. The process in cases of chronic subinvolution is partly physiologic, partly pathologic. Chronic subinvolution presents an exaggeration of normal physiologic involution, either with or without infection. It is chiefly ascribable to an endocrine factor except in those cases in which there is histologic evidence of infection, notably round cells, plasma cells, and increased connective tissue.

All clinicians are conversant with the appearance of a massive, hypertrophic, badly retrodisplaced uterus in a woman who has borne many children. This may be cited as an example of chronic subinvolution, but it may equally well be called diffuse hypertrophy. Similarly, in lesser degree, a badly retrodisplaced nulliparous uterus may also present a picture of diffuse hypertrophy. Microscopically, an excess of elastic tissue characterizes chronic subinvolution, whereas diffuse hypertrophy presents, theoretically, a proportionate increase in the various elements of the uterine wall, i.e., overgrowth of the muscle, the connective tissue, and the blood vessels. If there is associated endometrial hyperplasia, overgrowth of the various tissues may well be due to an endocrine factor. Changes of this sort, involving all elements of the uterus, are readily produced by prolonged excessive administration of estrogens.

A variant from chronic subinvolution and diffuse hypertrophy of the uterus is chronic metritis. Use of this term is preferable in those instances in which there is a grossly evident infection of the tubes, ovaries, or pelvic cellular tissues, or a history of puerperal or postabortive infection, histologic examination of the uterus presenting the usual residual evidence of an inflammatory process.

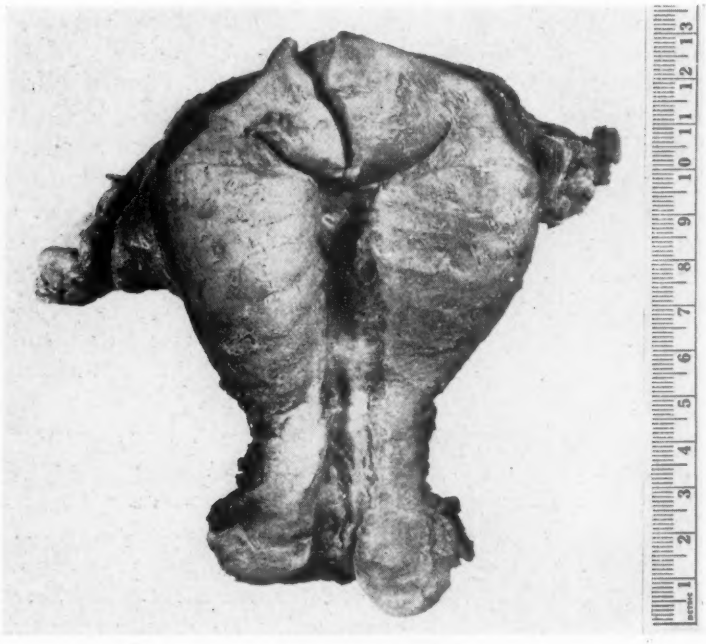

Fig. 1.—Hypertrophy of the uterus, the entire corpus involved. Length 13 cm., greatest breadth 9 cm., thickness of wall of body of uterus 3.8 cm. A typical instance of hypertrophy of connective tissue and uterine musculature, the blood vessels numerous and prominent with marked increase in connective tissue and elastic fibers evident on microscopic examination.

Fig. 2.—Hypertrophy of the uterus. Section through entire thickness of uterine wall showing (*C*) connective tissue replacement of musculature of outer third of uterine wall, (*M*) hypertrophy of remaining musculature, (*E*) hyperplasia of endometrium (trichrome stain). (×2½.)

Fig. 3.—Hypertrophy of uterus. Section shown in area indicated by square in Fig. 2, revealing massive hypertrophy of elastic tissue (Verhoeff metanil yellow stain). (×43.)

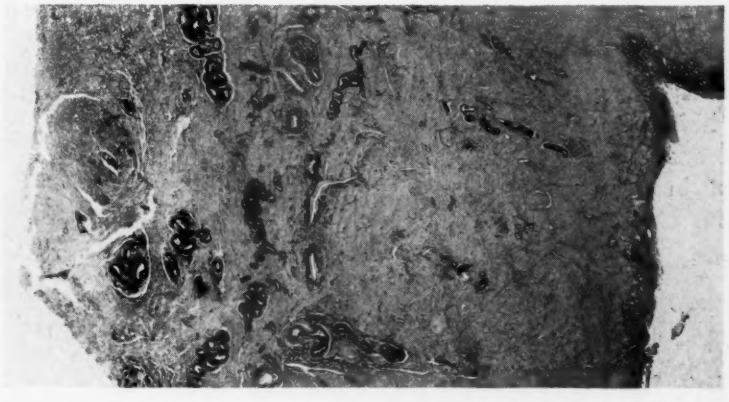

Fig. 4.—Hypertrophy of uterus, section through uterine wall. Hypertrophy of vascular and perivascular elastic tissue (Verhoeff-Van Gieson stain). (×2½.)

Diagnosis of Hypertrophy of the Uterus

The usual symptoms are prolonged or excessive menstruation, pelvic pressure with more or less aching discomfort, and increased vaginal discharge.

Examination reveals an enlarged uterus, which is usually heavy and often retrodisplaced and is difficult to differentiate on bimanual examination from adenomyosis of the uterus or diffuse enlargement from deeply buried myomas. Differentiation from carcinoma of the body of the uterus is sometimes difficult, occasionally even after examination of uterine curettings in those cases of hypertrophy with marked endometrial hyperplasia.

Histologic diagnosis of the various types of uterine hypertrophy is facilitated by differential stains. With routine hematoxylin and eosin stain, enlarged and thickened blood vessels and the amount of perivascular connective tissue are readily recognized, but accurate determination of the relative proportion of connective tissue and muscle cells is not simple. A trichrome stain, similar to the Mallory stain, developed in our laboratory by Miss Milligan, helps to solve this difficulty; the muscle cells and nuclei are stained red by acid fuchsin, the connective tissue clearly distinguished by fast green, the blood cells revealed in various shades of orange by orange G. In this connection, it is to be noted that differential stains must not be depended on implicitly, because degenerated tissue produces peculiar staining reactions and may lead to errors. Elastic fibers are recognized solely by special stains. Of these, the Verhoeff, preferably with metanil yellow counterstain, has been most satisfactory in our hands in the staining of formalin-fixed tissues. The orcein-Van Gieson stain has been less dependable for tissues fixed in formalin.

The more we study enlarged uteri, the more apparent it becomes that various gradations of hypertrophy are encountered in most instances and that pure subinvolution or true diffuse hypertrophy or hypertrophy due solely to metritis or to endocrine disturbance is unusual.

Treatment

Curettage may be required for differential diagnosis, and, strangely enough, it is sometimes beneficial. If more important surgical intervention is required, one should hesitate to perform corrective operations for uterine displacement in these cases unless childbearing is an important issue; removal of the offending organ by subtotal or complete hysterectomy is the procedure of choice.

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ANEURYSM OF THE SPLENIC ARTERY WITH RUPTURE, A RARE COMPLICATION OF PREGNANCY

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ANEURYSM of any sort is a rare complication of pregnancy. Aneurysms as a rule are found in individuals who are older than the great majority of expectant mothers. Aneurysms of the aorta of any sort are uncommon and aneurysms of its branches make up an extremely small part of the total of all aneurysms.

The following case, which illustrates a complication extremely rare during pregnancy, is reported.

A woman, aged 28 years, gravida iii, entered the hospital at the end of the seventh month complaining of severe upper abdominal pain. There was no external hemorrhage. Abdominal and pelvic examination were quite negative. All the usual signs of severe blood loss were present. She entered in the afternoon. On the following morning her condition was worse and heart tones were no longer to be heard. At this time she complained of tenderness over the uterus. Because it was feared that a premature detachment of the placenta might have occurred, it was decided to empty the uterus. This was done by vaginal hysterotomy. A dead fetus was removed but no sign of detachment was found. Transfusion was done. About midnight of this day sudden collapse followed by death occurred. Wassermann was negative.

The autopsy disclosed a massive hemorrhage into the peritoneal cavity, there being about 3½ liters of blood present. An enormous retroperitoneal hematoma was found which extended up to the level of the kidney. The aneurysmal sac was 1.5 cm. in diameter and contained clotted blood adherent to the lining of the sac. Blood had escaped at first from the wound in the aneurysm into the lesser peritoneal sac and later into the general peritoneal cavity. The wall of the aneurysm showed areas of necrosis in the intima and adjacent media. The tissue in these places was infiltrated with leucocytes and the elastic tissue was completely lost. Sections stained by the Levaditi method show no spirochetes.

A second case of aneurysm of the splenic artery not associated with pregnancy was seen recently on the medical service in this hospital. This patient was a woman of 62 years. She entered, complaining of abdominal pain unrelated to anything. After a number of days of observation, during which the cause of the pain remained undetermined, operation was decided upon. Exploration disclosed a mass in the upper right abdomen which was found to be an aneurysm of the splenic artery. This was removed, the artery being ligated on both sides of the arterial enlargement. The mass which was removed was 2 by 1.3 by 1 cm. It was smooth and yellow and consisted of the wall of a cystic cavity. There were extensive areas of calcification in the wall and marked thickening of the intima. Kline test was negative. Death followed in a few hours.

Baumgartner and Thomas, in 1924, stated that forty cases could be found in all available literature in fifty years. Of these, 19 were males, 16 females, and in 5 cases the sex was not stated. The size of the aneurysm in this series varied from the size of a cherry to that of a hen's egg. Of the entire number, 33 were first found at autopsy. The relationship between the sexes is interesting, inasmuch as the number of men and women approaches equality. The incidence of all aneurysms in males is five times that in the female. Garland, in 4,100 autopsies at the Massachusetts General Hospital, found only three aneurysms of the splenic

artery. Sperling, writing in 1940, found only three cases which had been diagnosed before operation or death. Lindboe, in 41,437 autopsies, reported 554 abdominal aneurysms, of which 26, or 0.05 per cent, were of the splenic artery. Anderson and Gray, writing in 1929, found 58 cases in the literature and reported an additional one. Machemer and Fuge, in 1939, found 24 additional cases in the ten years which had elapsed since the publication of the paper of Anderson and Gray. Schroeder, who wrote in 1918, reported 20 aneurysms of the splenic artery in a series of 32,768 autopsies. All reports indicate that the condition is a very rare one and that its coincidence with pregnancy is still more rare.

Published reports indicate that it is most frequent in the third decade, although the fourth, fifth, sixth, and seventh show nearly as many.

The cause cannot be stated too definitely. Binder says that syphilis, except in the case of aneurysm of the aorta, does not play a part. The study of the reported cases would indicate that calcification of the arterial wall, with attendant weakening, is of etiological importance. Ponfick suggests that endocarditis is as important etiologically and believes that an embolism at the point at which an artery branches in loose supporting tissue may be the determining force which produces the aneurysm.

Recognition of the condition is extremely difficult. Sperling suggests three suggestive signs which may help in determining the presence of a splenic aneurysm. These are: (1) left upper quadrant pain, (2) a systolic bruit over a palpable tumor mass, and (3) a pulsating filling defect in the greater curvature of the stomach as shown by the x-ray.

In the great majority of the reported cases diagnosis has not been made. It has been confused with cholelithiasis, cholecystitis, pancreatitis, and ectopic pregnancy. It may also simulate perforated gastric ulcer, mesenteric thrombosis, or a ruptured viscus. Two cases of successful preoperative diagnosis are reported by Högler who found the pulsation of the mass by fluoroscopy.

In many of the reported cases, blood was found in the stool, and Lower and Farrell suggest the examination of the stool for undigested fat in order to detect a lessened pancreatic activity which may be due to the pressure of the mass upon the pancreas.

In the great majority of the reported cases, massive hemorrhage was found in the peritoneal cavity. In the first case here reported, in addition to an enormous retroperitoneal hematoma, there was a large amount of blood in the peritoneum. In some cases the hemorrhage did not terminate life at once. A primary hemorrhage took place, in many cases into the lesser peritoneal cavity. In the second case seen in this hospital, the patient remained in the institution fourteen days before death, which took place on the same day as the operation which was finally undertaken.

As to the prognosis, Lower and Farrell found that of 15 cases in the literature upon which operation had been done, 7 had recovered. If surgical therapy is to be attempted, it should be either the removal of the aneurysm, with the excision of the spleen as well, if necessary, or the ligation of the splenic artery. The latter procedure will carry with it an aseptic necrosis of the spleen which does no harm. The ligation of the splenic artery in experimental animals has

proved to be safe, and recovery has followed the ligation of the artery in human beings. In those cases in which tamponade was resorted to, death followed invariably.

In both the cases here reported and in that of Sered and Steiner, in both of which the patients were pregnant, death ensued. In the series of Baumgartner and Thomas, one case was found in which an aneurysm of the splenic artery ruptured during labor. The condition is evidently a most serious complication of pregnancy. It would seem that it is even more serious during pregnancy than at other times for two reasons. First, the difficulty of arriving at an accurate diagnosis at any time, even though the abdominal field may not be obscured by the large tumor incident to an advanced pregnancy. Second, the operative attack, without which the issue is nearly always fatal, is rendered far more difficult and dangerous by the presence of the pregnancy. In our own case, had it been possible to have recognized the presence of the aneurysm, after emptying the uterus by vaginal hysterotomy, we might have proceeded to deal with the aneurysm surgically. The condition of the patient at that time would have rendered the procedure hazardous, even without the preceding obstetric surgery. If the pregnancy is beyond the first four months, it would seem essential to do away with the uterine mass before attempting the upper abdominal surgery. Unless the cervix is easily accessible and not too long, the easiest way of doing this would be by abdominal section, preferably the low cervical type of hysterotomy. If the uterus could be emptied easily from below, it would have the advantage of avoiding two abdominal incisions.

In cases in which upper abdominal pain comes on suddenly without other obvious explanation, it is suggested that the possibility of aneurysm of the splenic artery be kept in mind. The triad of signs suggested by Sperling may be useful. If a palpable tumor is present, one should listen for a bruit, and the presence of a pulsating tumor, indicated by fluoroscopic examination of the stomach, may be very valuable. While the complication is a rare one, the fact that it is fatal, and that immediate recognition and efficient surgical attack may serve to rescue the patient, should cause the obstetrician to keep in mind the possibility, if not the probability, of such a condition and to recognize it if possible.

In the series of cases reported by Machemer and Fuge, are found eight in which the aneurysm was a complication of pregnancy. Their paper appeared in 1939. Since that time four additional cases have been reported to which the case noted herein may be added, making a total of 13 cases in the entire available literature since 1939. While the condition is not a common one, it occurs with sufficient frequency to make a familiarity with its symptoms desirable. Enough cases have occurred in pregnancy that it may well be kept in mind by the obstetrician when upper abdominal pain occurs, especially if accompanied by the signs of loss of blood.

Without active therapy, even in the absence of pregnancy, the prognosis is very poor. The outlook in general may be indicated by the analysis given by Machemer and Fuge. In 25 cases in which no surgical treatment was attempted, there were 18 deaths, a mortality of 75 per cent. In 13 cases in which surgical

treatment was tried, there were 7 deaths, a mortality of 47 per cent. In some of these cases the treatment was merely tamponade. In eight cases in which the aneurysm was removed, or in which the splenic artery was tied, there were two deaths, a mortality of 25 per cent. The numbers quoted are not sufficiently large to give a wholly accurate statistical picture but they strongly suggest that removal of the aneurysm or ligature of the artery is the best method of management. Tamponade is unsatisfactory and is accompanied by a high mortality.

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THE SEARCH FOR THE FEMALE SEX HORMONES

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HAVING taken part for more than twenty years in the search for and identification of the female sex hormones, I feel qualified in giving a vivid picture of this quite romantic chapter of endocrinology. Some of the functions of the gonads have been known since prehistory, as evidenced by the fact that castration was practiced on both the male and female of animal and human species. The knowledge that castration produced certain other changes, besides the abolition of the sex cycle, was accepted, as shown by history, both medical and lay. Yet as late as 1912, two prominent members of the American Gynecological Society did not hesitate to put themselves on record by stating boldly that, in their opinion, no proof has been given that the ovary had any function in addition to that of supplying ova.

In 1893, Regis, of Bordeaux, evidently influenced by Murray's success with thyroid substance, made a glycerin mash of animal ovaries and injected the mess subcutaneously into human beings afflicted with melancholia and other nervous diseases. He reported many striking successes. Actually, the distinct evidence of an internal secretory effect of the ovaries was first given simultaneously and independently by two Viennese workers: the one, Halban, an active and prominent gynecologist; the other, a laboratory man, Knauer, in 1898. They succeeded in re-establishing the sex cycle by reimplanting ovaries in rodents and monkeys. The next important milestone hails from Breslau. Ludwig Fraenkel, who is still active, now residing in Uruguay, in 1903 reported that removal of the corpus luteum invariably produced abortion in the pregnant rabbit. He had been led to undertake this research by his teacher, Borne, who died before completing his experiments. The so-called nidatory theory of the corpus luteum has been substantiated by all subsequent work. In 1905, Halban published an extremely important contribution, describing the internal secretory function of the placenta. His whole thesis was based on clinical observation. It covered the continuation of nidation, the breast changes, the uterine hyperplasia, and other symptoms associated with pregnancy. He based all of his conclusions on numerous clinical observations. In the years which have elapsed, all the experimental work and increase in knowledge has authenticated practically every point that he made. From 1908 on, working in Philadelphia, Leo Loeb undertook numerous carefully planned and well-controlled experiments on guinea pigs. By means of these he showed that the corpus luteum not only had the function ascribed to it by Fraenkel, of insuring the nidation of the ovum, but also that the corpus luteum controlled the periodicity of the sex cycle. Moreover, his experiments showed that the nidatory function was exerted through the production of a maternal portion of the placenta, both embryonal and maternal placenta being necessary for successful nidation and continuation of pregnancy.

It should be noted that during these preliminary years practically the entire attention of investigators was focused on the corpus luteum, which was considered the main, probably the sole, functional portion of the ovary. It is true that in 1906 the well-known physiologist, Starling, who had introduced the clear concept of "hormone," as observed in the production of gastric secretin, published a paper, with Lane-Claypon, on the factors which determine the growth and activity of the mammary gland. This paper, which postulated that the fetus and placenta contain a hormone which activated the breast, drew correct conclusions on entirely erroneous experimental data. The reason for their error was due to the fact that they were unaware of the breast changes occurring in the rabbit during the normal sex cycle. Unger and I drew attention to their error which, however, these distinguished investigators never acknowledged or conceded. It may be said that during this decade, inconclusive results were obtained with extracts of ovaries and placenta because practically all of the extracts used for experimental purposes were aqueous and, therefore, as our subsequent increase in knowledge has shown, failed to dissolve the lipoid soluble sex hormone. Consequently, the greatest advances were made by morphologic investigations throughout the cycle such as those of Leo Loeb. Another group of investigators who advanced our knowledge were the Frenchmen, Ancel and Bouin, who, from 1908 on, investigated the sex cycle, correlating ovarian and uterine, and mammary histological findings. They devised a method to produce what was then not yet known as "pseudopregnancy" in the rodent. They produced this by cohabitation with vasectomized males. The sex act caused the pseudopregnancy and therefore persistence of the corpus luteum. Investigations on human material threw additional light on the cycle. Hitschmann and Adler, Mayer, Albrecht and others correlated ovarian and uterine endometrial cycle by comparing specimens obtained at different intervals.

A new era of investigation dates from the time that an obscure instructor in chemistry in a French high school, Iscovesco, used various lipoid solvents in obtaining extracts from ovary, placenta, and various other organs. These extracts, which were fractionally separated by various nonmiscible solvents, produced very definite uterine changes in immature or castrated experimental animals. Throughout these researches which were extended by others, Herrmann in Vienna and also Fellner, Frank and Rosenbluth in New York, it was shown that corpus luteum extracts produced marked hyperplasia in the uterus of castrates. A variable reaction was obtained in the mucous membrane; sometimes there was marked glandular hyperplasia such as was noted by the morphologists in pseudopregnancy; sometimes this was absent. An explanation for this discrepancy was not discovered for many years.

In 1916 I came across an obscure observation of Bucura's, dating from 1908, which had attracted no attention whatever. In a resection of the ovaries of rabbits, in one case he found nothing but a single follicle which had developed, the rest of the ovary having been resected. He noted that the uterus of this animal at autopsy showed marked hyperplasia. This observation was buried in the literature for many years. Having worked with numerous associates in try-

ing to obtain a concentrate of the corpus luteum and to purify this, we reached a certain point, but, after that, further purification was unaccompanied by increased activity. Partly because I remembered Bucura's observation and partly because it seemed likely that the follicle fluid should have some function, in 1917 I obtained a considerable number of sow's ovaries, aspirated the fluid from the ripening follicles, and injected it into immature rabbits. A surprisingly rapid and marked hyperplasia of the uterus developed, not accompanied by an excessive arborization of the mucous membrane glands. Because of interruption produced by my entrance in the Armed Service and subsequent ill-health, I failed to publish this finding until 1922, although I had placed the record of it in care of the Crocker Cancer Research Laboratory in 1917. I published this observation in 1922 in the *Journal of the American Medical Association*. This was really the first definite proof offered that another constituent of the ovaries besides the corpus luteum produced a hormone. This concept was popularized and widely disseminated in 1923 by Allen and Doisy, who miscalled the follicle fluid the "ovarian hormone." Really, their main contribution at that time, a major one, was the rodent vaginal smear test as a qualitative test for estrogenic activity. As soon as this test became available, the slow, expensive, and tiresome test, based on gauging the size of the rabbit uterus, became obsolete, and speeding up the search for estrogens was immeasurably increased.

Even with the Allen and Doisy test available, the progress in isolating the active substance of the ovary did not gain greatly until Sigmund Loewe, previously of Dorpat, later in Frankfurt, discovered that great activity resided in the urine of pregnant women. Thus a solution of the hormone, let us call it by its present name of "estrogenic," in aqueous medium, eliminated the innumerable complicating contaminants present when the hormone was obtained from either ovarian or placental material. Doisy, and almost simultaneously Butenandt, isolated, crystallized, and determined the chemical structure of estrone. Within a surprisingly short time not only estrone but estriol and estradiol were isolated. The biochemists did an amazingly quick and thorough job so that today we know that the ovary produces the strongest hormone, estradiol, that during its metabolism it probably is reduced to estrone and estriol which have less activity, and is excreted in the form of compounds of glucuronic acid and sulfuric acid in the urine and feces. This is not the place to enter into details which are so readily available elsewhere.

In 1928, W. Allen and Corner went to work in purifying the corpus luteum extract, and gave clear-cut chemical evidence of the presence and activity of the corpus luteum and its effect upon the breasts and uterus. At this time they showed that the arborial glandular mucosal changes were corpus luteum in nature. They not only confirmed the work of the morphologists, Loeb, and Bouin and Ancel, etc., but they also gave a clear-cut experimental proof that the Borne-Fraenkel theory was a fact and that pregnancy after removal of the corpus luteum in ovaries could be continued by means of extracts containing progestin.

To date, the concluding chapter in the search for the sex hormones includes the discoveries by Philip E. Smith, and simultaneously and independently by

Aschheim and Zondek in 1926, that the anterior lobe of the pituitary contains the gonadotropic hormones which actually activate both the male and female gonad, proving that the gonads are, so to speak, stars of second magnitude. Whether these are one or two gonadotropic hormones, the one follicle stimulating, the other luteinizing, is still a moot question, and although considerable purification has been obtained, the integrally protein nature of these hormones has so far defied full identification.

In this very brief and summarized personal review, the innumerable building stones which were necessary for the construction of the entire picture could not be mentioned in detail. The first ten years of this century saw important but rather disconnected work performed, partly on animals, but largely histological in nature. The first half of the second decade was marked by research with crude extracts. It was not until the biochemists came to the aid of the gynecologists and physiologists that rapid and conclusive advances were made. There is still, however, much to be clarified in this fascinating subject.

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THE ROLE OF PORRO CESAREAN SECTION IN MODERN OBSTETRICS

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IT WAS in 1876 that Porro first removed the uterus following cesarean section. He did this in the hope of reducing the appalling mortality which was associated with the operation prior to the introduction of the Sänger technique. The deaths associated with the old operation, when the uterus was not sutured, practically always resulted from hemorrhage or infection, and Porro sought to eliminate these factors by the removal of the uterus. While the immediate results were not brilliant as compared with modern-day surgery, they at least presented a definite improvement over those obtained with the old operation. Thus, in 1882, Godwin collected 134 cases with a maternal mortality of 55.8 per cent, a very high figure but still representing an improvement over the results previously obtained from the original operation.

Introduction of the Sänger technique brought about further striking improvement in maternal results and also reduced materially the necessity for performing the Porro operation, which, after all, is a multilating operation which permanently sterilizes the woman. While Porro's original technique of suturing the cervical stump to the lower angle of the abdominal incision is no longer followed, but rather a subtotal or total hysterectomy by modern surgical methods is done, yet his name is still attached to the procedure and such an operation is generally spoken of as a Porro cesarean section.

Although the introduction of the Sänger technique, together with the application of, first antiseptic and, later, aseptic measures, reduced the cesarean section mortality very materially, the results still left a good deal to be desired. This was due largely to the fact that a long time elapsed before it was recognized that the classical cesarean section is a dangerous procedure if not done before labor sets in or at the very onset of labor. Introduction of the technique of the lower cervical cesarean section and the various forms of extraperitoneal operations, however, today permit reasonably safe abdominal delivery for many women whose lives would be jeopardized by performing the classical operation. These techniques have also reduced materially the necessity for performing the radical operation.

While this is true, it is also a fact, however, that, on occasion, removal of the uterus after cesarean section will be very definitely indicated. Indicative of the decreased frequency for the necessity of this operation, comparison may be made between a series from the clinic of the late J. Whitridge Williams, reported by Harris in 1922, and the series presented herewith. In the former series of 223 cesarean sections the uterus was removed in 64 instances, or 29.5 per cent, while in our series of 355 cesarean sections of various types it has been found necessary to remove the uterus only 31 times, an incidence of 8.7 per cent.

The indications for this operation are relatively few but they are of great importance. In the present series there were four particular indications for which the operation was done: namely, myomas of the uterus, uncontrollable hemorrhage, severe intrapartum infection, and in order to effect sterilization.

Record of Cases at Strong Memorial Hospital

Myomas of the Uterus.—In ten women the uterus contained myomas of such a size and in such position as to demand delivery by cesarean section. At the time of operation the myomas were found to be of such size or so numerous as to preclude myomectomy, so the uterus was removed. All made excellent recoveries and the infants all survived (one case of twins). It is interesting to note that six of the women were elderly primiparas—over 35 years of age. In each instance the operation was done as an elective procedure and before the onset of labor.

Uncontrollable Hemorrhage.—In seven women it was found necessary to remove the uterus after cesarean section on account of this indication. In five of these women the cesarean section was done on the indication of abruptio placentae, and following the emptying of the uterus, as often happens in such hemorrhagic and infiltrated uteri, bleeding continued to a degree to endanger seriously the patient's life and could not be controlled by the usual measures. Under the circumstances, nothing remained to be done except to remove the uterus in order to avoid a tragedy.

Differences of opinion exist as to the best method for the treatment of acute premature separation of the placenta with concealed hemorrhage, but one of the advantages offered by delivery by cesarean section is the opportunity to observe the uterus, its condition and its behavior after emptying, preserving it when possible, but removing it without hesitation if bleeding cannot be controlled.

In two other women on whom classical elective cesarean sections were done, one on a young woman for contracted pelvis, the other on an elderly primipara of 42 years, uncontrollable bleeding occurred after delivering the child and placenta, so that it was necessary to sacrifice the uterus in these two women—a tragic circumstance in the young woman but not of such great significance in the older woman. It is interesting to note that in these two operations removal of the uterus was deferred to the last possible minute; in fact, in both instances the uterine incision had been sutured before it was recognized that removal of these uteri was demanded on account of their complete failure to contract. From one of these, after removal, 1,000 c.c. of blood were collected from the cavity. This represents a difficult situation, requiring a quick decision but at the same time the greatest nicety of judgment. In the uterus not damaged by hemorrhagic infiltration, as in abruptio placentae, the problem of uncontrollable hemorrhage is fortunately encountered very infrequently. In this group all the women made excellent recoveries, but five infants were stillborn. These stillbirths occurred in the five women presenting abruptio placentae, the infants being dead at the time the operation was begun.

Intrapartum Infection.—In nine women the uterus was removed following cesarean section on account of the existence of a severe intrapartum infection at the time the operation was done. This is the type of case in which the operation was formerly most frequently employed, and is also the group in which modern methods of obstetric practice should materially reduce the necessity for the operation. Fewer neglected cases are seen than formerly, and proper resort to lower cervical and extraperitoneal section in suitably selected cases should also reduce the necessity for resort to the more radical operation.

In reviewing this particular group of nine women, it would appear that three of them might possibly have been delivered with reasonable safety by some form of extraperitoneal cesarean section. These are to be regarded as potentially infected rather than frankly infected. The others, however, had had various types of manipulation from below before the operation was done and presented frank evidence of intrapartum infection of a serious nature.

Even with the advent of the sulfonamides and penicillin, admittedly valuable and forceful agents for combating infection, it would seem to me an undue risk to leave the frankly infected uterus in situ after cesarean section.

In this group all the women recovered, but one developed a wound infection which necessitated a secondary closure.

There were four stillbirths or neonatal deaths, two from atelectasis, one double monster on which evisceration had been attempted before operation, and one in connection with a placenta previa, the infant being dead at the time of operation.

Sterilization.—In five women the uterus was removed as a means of effecting sterilization at the time cesarean section was done for other reasons. This is not the usual method for effecting sterilization nor, on the whole, is it the most desirable. On the other hand, it is possible on occasion to obtain permission for hysterectomy when permission for resection of the tubes would be refused. Also, on occasion, menstrual disturbances prior to the pregnancy may warrant removal of the uterus, or the patient may request it.

All five of these women made good recoveries, but one baby failed to survive, due to prematurity. This neonatal death occurred in the case of a woman previously delivered by cesarean section, the operation being followed by a serious infection. On admission, she had a deeply furrowed uterus which impressed us as being unable to withstand further distention although the baby was as yet obviously small. Sterilization, by removal of the uterus, was at her request. The child weighed only 1,200 grams and died in twenty-four hours.

TABLE I. SUMMARY OF CASES

INDICATION	NO. OF CASES	MATERNAL DEATHS	FETAL DEATHS
Myoma uteri	10	0	0
Uncontrollable hemorrhage	7	0	5
Intrapartum infection	9	0	4
Sterilization	5	0	1
Total	31	0	10 or 32.2%

Summary and Conclusions

A series of 31 women in whom cesarean section followed by supravaginal amputation of the uterus (Porro cesarean section) was performed is presented. The maternal results were uniformly good, there being no maternal deaths. That, of course, is not to say that the operation is without mortality, as the series is a small one. There were 10, or 32.2 per cent, stillbirths or neonatal deaths. None of them can be attributed to the operation, as in seven instances the infant was known to be dead at the time the operation was done and had died as the result of the condition for which cesarean section was indicated. Two mature infants died of atelectasis and one infant of prematurity.

This operative procedure still has an important place in obstetric operative procedures, though the necessity for it has decreased materially following the introduction of other operative techniques, such as the low cervical cesarean section and the various forms of extraperitoneal operations. Also, with improved prenatal care and increasing hospitalization of obstetric patients, fewer neglected cases are seen.

The particular indications for removal of the uterus after cesarean section are found to be: (a) Myomatous uteri containing myomas of such a size and in such a position as to necessitate cesarean section in the first place, and when

myomectomy is precluded. (b) Uncontrollable hemorrhage when removal of the uterus is necessary as an emergency lifesaving measure, often in association with abruptio placentae but occasionally encountered apart from this. (c) The presence of frank intrapartum infection when cesarean section is done. It is in this group in particular that a decrease in the necessity for the removal of the uterus has occurred, and further reduction should be possible. (d) As a means of effecting sterilization when sterilization is indicated and where for some reason it may seem preferable to remove the uterus rather than to resect the tubes.

No examples of ruptured uterus requiring hysterectomy are included in this series as this would seem to be an entirely separate problem.

ECTOPIC GESTATION

The Diagnostic Value of Cul-de-sac Aspiration

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ECTOPIC gestation or extrauterine pregnancy is more often overlooked and more often diagnosed when not present, than any other serious pelvic lesion.[1] Farell and Scheffey[2] of Jefferson Medical College reported 157 cases of ectopic gestation from Sept. 21, 1921, to Sept. 1, 1942. A correct diagnosis was made in 76 per cent of the cases. Child and Douglas[3] reported three normal pregnancies and three incomplete abortions diagnosed as ectopic pregnancies. Torpin[4] recently reviewed the literature and showed an incorrect diagnosis ranging from 14.8 per cent to 47 per cent from fourteen different clinics with an average of 27.3 per cent incorrect. These reports from the best clinics in the country clearly show how difficult it is to make a correct diagnosis.

We have divided ectopic gestation into two varieties—the typical and the atypical; the typical comprises 40 per cent of the cases, the atypical 60 per cent. The history of the case, symptoms, and physical signs stand out first in importance in making a diagnosis. It is a disease that occurs only during the sexual life of the woman. It is most common between 20 and 30 years of age. Next in frequency is the fourth decade. A small percentage of cases is found below 20 and above 40 years of age.

A preceding history of sterility before the occurrence of an ectopic gestation is quite common. It is usually found in women of low fertility. A history of pelvic inflammatory disease, infection following labor or abortion, or an infection following abdominal section for a ruptured appendix is quite common. The Vanderbilt cases showed pain present in 100 per cent; a missed period in 90 per cent; a bloody vaginal discharge in 89 per cent, and a mass in the pelvis in the typical variety in less than 50 per cent and present in the atypical in over 90 per cent.

The typical case is characterized by a violent pain in the abdomen associated with a bloody vaginal discharge and shock. Usually there is a history of a missed period. Shoulder pain is present in 25 per cent of the cases and is a most valuable symptom. Rigidity of the abdominal muscles is generally absent, but tenderness on palpation, either general or localized, is present in the lower quadrant.

On vaginal examination we note a pelvic mass is absent in about 55 per cent of the cases. A mass may be palpated if the free blood present has formed clots or if the pregnancy is sufficiently large to be palpated. If sufficient blood has

been lost, there will be a decrease in the hemoglobin and red blood cells which, in many cases, is quite marked. The white blood count rarely goes above 15,000, although in the massive hemorrhage this may go to 20,000 which decreases as the blood is absorbed. The pulse rate is accelerated and the temperature is subnormal. Preparation should be made for operation and blood should be administered to bring these patients out of shock while the operating room is being prepared. The transfusion needle should be left in place in order to give more blood during or after the operation. In those institutions in remote areas that do not maintain a blood bank or have plasma available or in those cases in which there is an Rh factor or an unusual type of blood, we would suggest autotransfusion, or reinfusion of the patient's own blood.

In 1923 I reviewed the literature on autotransfusion, and strongly advise the use of this procedure.[6] We cannot be too emphatic in urging in the typical case a quick diagnosis and an early operation.

In the atypical variety the patient is not in shock. The sighing respiration and the blanched appearance are absent. The thready pulse and the subnormal temperature are not present. It is in this variety that time can be taken to make use of procedures so useful in arriving at a correct diagnosis.

We have reviewed the cases of ectopic gestation in the Vanderbilt University Hospital from Sept. 1, 1925, to July 1, 1945. This study comprises an analysis of 105 patients who were admitted or discharged with the diagnosis of ectopic gestation. Sixteen patients were admitted with a diagnosis other than ectopic gestation, but extrauterine pregnancies were found at operation. Eighteen patients were admitted in shock. Seventeen of these had extrauterine pregnancy. The other patient had a ruptured corpus luteum with intraperitoneal hemorrhage. The remaining 71 patients were admitted with a suspected diagnosis of ectopic pregnancy.

The common conditions in which a mistaken diagnosis is often made are: pelvic inflammatory disease, abortion, a cyst of the corpus luteum producing a positive Aschheim-Zondek test, a normal pregnancy associated with a large corpus luteum, a small ovarian cyst which is inflamed and associated with torsion of the pedicle, a ruptured Graafian follicle or corpus luteum producing an intraperitoneal hemorrhage with shock, a normal pregnancy with a soft uterine wall with an extreme dextrorotation, and abdominal pregnancies. A mistaken diagnosis may also be made of the following: pregnancy in the uterus associated with a tubal pregnancy, pregnancy in a bicornate uterus, tubal pregnancy associated with a cyst in a case which had formerly had one tube removed for ectopic gestation. The discovery during operation of ectopic gestation for the mistaken diagnosis of appendicitis is not an unusual mistake. Pregnancy tests are of value but a diagnosis should not be dependent on this test. There are many conditions which will produce a positive pregnancy test when pregnancy is not present. The most common ones are: chorioepithelioma, hydatidiform mole, missed abortion, teratoma of testicles, embryonal adenocarcinoma, seminoma, myosarcoma, teratoma of ovary, luteum cyst, granulosa-cell carcinoma, para-ovarian cyst, and certain forms of psychosis.

We might add that any case which is diagnosed as appendicitis is entitled to a pelvic or rectal examination and a careful review of the menstrual cycle before operation.

In pelvic inflammatory disease, pain usually makes its appearance at the time of the period or just after it. The history of the case, signs of gonorrheal infection, smears, culture, sedimentation rate, and leucocyte count are of value, but at times deceptive. In gonorrhea the leucocyte count will run between 15,000 and 20,000. In ectopic gestation it is usually below 15,000. The temperature in ectopic is rarely above 102° F. In pelvic inflammatory disease it may run as high as 103° F. The sedimentation rate is more rapid than in ectopic. The pregnancy test is often positive in ectopic and in gonorrhea it is negative. Gonorrheal salpingitis produces a bilateral adnexal mass with an associated lower abdominal rigidity, whereas ectopic produces a unilateral mass and the rigidity, if present, is on the affected side. In gonorrhea the pain is constant; in ectopic it is intermittent. Culture for gonococci is a laboratory procedure of great value and should always be used in a suspected case. The finding of blood in the peritoneum should clear up the diagnosis.

Abortion is easily mistaken for ectopic gestation. Curettage may assist in the diagnosis by finding chorionic villi or decidual membranes in the scrapings. Some advise its use as a routine measure and as an aid in the diagnosis of the atypical case. We do not concur in this view and believe a curettage for diagnostic purposes in a case of partial rupture or tubal abortion may bring on an intraperitoneal hemorrhage with possibly a fatal result. When one has a suspected case of abortion, ectopic should be ruled out; and in suspected cases of ectopic, abortion must be eliminated.

Cullen's sign or blue navel indicates an intraperitoneal hemorrhage. It is rarely found.

Israel[5] reported six cases of corpus luteum cyst and in two of these a positive pregnancy test was present. In the Vanderbilt series one case of corpus luteum cyst with a positive pregnancy test was found.

A ruptured Graafian follicle usually occurs at the midmenstrual interval. A ruptured corpus luteum occurs just before the onset of menstruation. A most confusing condition is a normal pregnancy associated with a soft uterine wall and an extreme dextrorotation. We recently had a case of this kind associated with a small fibroid the shape and size of the uterus in the pelvis. A mistaken diagnosis was made from the impression that the fibroid was the uterus and the dextrorotation of the normal pregnancy was either a cyst with torsion or perhaps an ectopic gestation. One pregnancy test in this case was positive, the other was negative. This unpardonable error would not have occurred if a pneumoperitoneum had been carried out, followed by x-ray.

South American surgeons have advised the use of an opaque substance injected in the uterus followed by an x-ray picture. They claim that this injection will not dislodge a pregnancy in the tube and that it will clearly show a pregnancy if present. We would not advise this procedure until time and further experience show it to be free of danger. We have found the injection

of carbon dioxide gas into the peritoneum through an abdominal puncture followed by an x-ray of the pelvis a procedure of great value in arriving at a diagnosis. It is free of danger but can be used only in those institutions where there is a close cooperation with the x-ray department which is trained in this technique. The peritoneoscope is an instrument which has a great future. It must be used by a man who has had experience and training. We gave up the use of this instrument during the war, due to rapid changes in the staff and the inability to assign one man to this particular duty.

We desire to emphasize especially in this paper the value of aspiration of the peritoneum either per vaginam or through the abdominal wall if conditions in the cul-de-sac make it not advisable to aspirate per vaginam. It is not an original procedure. It is one that we have used not only in making a correct diagnosis, but also in avoiding unnecessary operations. The procedure is not time consuming and can be used in any institution or hospital or even in the private home if necessary. If the aspirated blood shows an absence of rouleaux formation and the erythrocytes show a crenated appearance, it signifies a hemorrhage into the peritoneal cavity.[7]

In obtaining blood from the peritoneal cavity we look for color, viscosity, presence of small clots, and clotting time. The old blood has a definite brownish tint. It is thinner than fresh blood and does not clot. We have usually used a size 17 needle, which is large enough to permit the aspiration of small clots.

Review of Cases

Of the 71 suspected cases of ectopic gestation admitted in good condition and presenting diagnostic difficulty (Table II), 42 patients, or 62 per cent, were found to have extrauterine pregnancies. Twenty-nine patients did not have ectopic pregnancies, but had some other difficulty summarized in Table I.

TABLE I

Corpus luteum cyst	6
Pelvic inflammatory disease including all diagnoses such as pelvic abscess, salpingitis, tubo-ovarian abscess, pyosalpinx, etc.	15
Follicle cysts	2
Undiagnosed	5
Metastatic adenocarcinoma of the cul-de-sac	1
	29

In 22 patients, puncture was performed (this includes two cases of abdominal puncture) and old blood was obtained. Twenty of these cases had extrauterine pregnancies, one had a ruptured follicle cyst with marked intraperitoneal bleeding, and one had an adenocarcinoma of the cul-de-sac. This gives us a diagnosis rate of 91 per cent. Of the fifteen cases that had cul-de-sac puncture, but no old blood was obtained, none were proved to be ectopic pregnancies. While it is always possible that some of them might represent tubal abortions, the fact remains that when laparotomies were performed on five of them, no ectopic was found. The remaining 34 cases were not subjected to cul-de-sac puncture and in 12 of them no ectopic gestation was found. To summarize: if we consider the presence of old blood obtained by cul-de-sac puncture a positive test for ectopic gestation,

and if we consider the absence of old blood as a negative test, we may say that in this series of 37 patients exposed to cul-de-sac puncture, there were no false negative tests and two false positive tests. In our hands, the cul-de-sac puncture when used as a test for the presence or absence of extrauterine pregnancy is accurate in 94.6 per cent of the cases. This compares very favorably with the correct diagnosis rate of 65 per cent for 34 cases that were diagnosed only by the usual clinical and laboratory means.

TABLE II

	NUMBER OF CASES	NUMBER CORRECTLY DIAGNOSED	NUMBER INCORRECT DIAGNOSIS	% CORRECT DIAGNOSIS
Cul-de-sac puncture and old blood obtained	22	20	2	91
Cul-de-sac puncture and no old blood obtained	15	15	0	100
No cul-de-sac puncture	34	22	12	65
Total	71	57	14	80.3

TABLE III

	NUMBER OF LAPAROTOMIES	UNNECESSARY LAPAROTOMIES	NECESSARY LAPAROTOMIES	% OF UNNECESSARY LAPAROTOMIES
Cul-de-sac puncture performed and old blood obtained	21	0	21	0
Cul-de-sac puncture performed and no old blood obtained	5	5	0	100
No cul-de-sac puncture performed	33	10	23	30
Total	59	15	44	25

Table III is most interesting. We have attempted to analyze the 71 cases to determine how many unnecessary surgical operations were performed because of a suspected diagnosis of ectopic gestation. An unnecessary laparotomy is defined as one performed for some pelvic pathology for which we would not have operated had a true diagnosis been known preoperatively. Twenty-one of these cases were operated on after a cul-de-sac puncture and in this group of patients no unnecessary surgical procedures were performed. In five cases in which no old blood was obtained, the surgeon ignored the cul-de-sac puncture and laparotomy was performed. In no case was any pathology worthy of surgery found. Thirty per cent of these operations without cul-de-sac puncture were unnecessary. We believe that the presence of old blood obtained by a cul-de-sac puncture is an absolute indication for surgery. The absence of old blood so obtained is a contraindication to surgery performed because of the suspected presence of an extrauterine gestation.

Howard Kelly many years ago advised colopotomy. It is a valuable procedure as an aid in making a diagnosis, but why carry out a major surgical procedure to obtain information that can be easily obtained by an aspiration per vaginam or through the abdominal wall. We consider aspiration the most valuable of all aids in making a diagnosis of doubtful cases of ectopic gestation. Next to aspiration we consider pneumoperitoneum and x-ray as a valuable aid.

All of us make mistakes. All of us occasionally do an unnecessary operation. We are of the opinion, however, that with a careful study of this most

interesting and sometimes fatal condition, giving due consideration to the history, the physical signs, the laboratory tests, x-ray, and especially aspiration, our margin of error will be greatly reduced.

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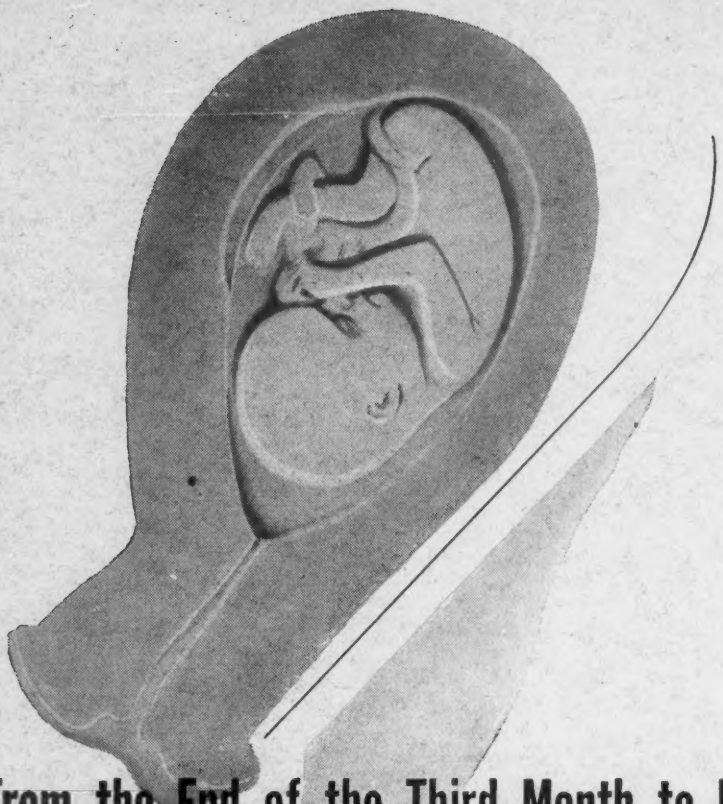

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1. E. D. Colvin et al: Am. J. Obstet. & Gynecol., 43:183, Feb. 1942.

2. N. M. Phatak et al.: Proc. Soc. Exper. Biol. & Med., 45:667, Nov. 1940.

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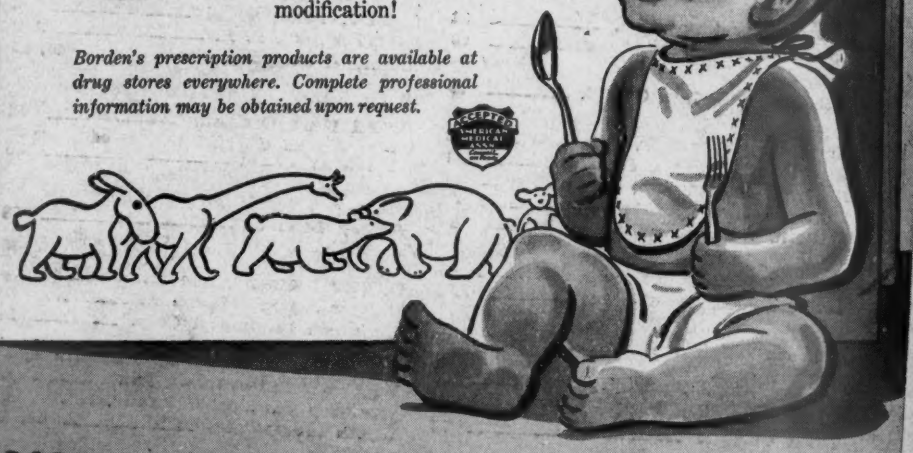

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